



PRESIDENT'S PAGE

Acute coronary syndromes and diabetes mellitus



Diabetes mellitus (DM) is a rapidly growing pandemic disease affecting more than 350 million patients all over the world.¹ In addition is one of the major risk factors for coronary artery disease and more than 40% of patients with acute coronary syndrome (ACS) have DM.^{2,3} Additionally, mortality in patients with ACS is 2–3 fold elevated in diabetic patients compared with non diabetic ones⁴ while in ACS both subdiagnosed diabetic patients and patients newly diagnosed with impaired glucose tolerance have increased 30-day mortality in comparison with non diabetic ones.⁵ Long lasting studies in diabetic patients with ACS have shown an increase of 1.8 fold the incidence of cardiovascular death and 1.4-fold increase in myocardial infarctions after 2 years than non diabetic ones.⁶

Specifically on patients after acute myocardial infarction with ST segment elevation (STEMI), compared to non-diabetics, diabetic patients present more slowly in the emergency department more often present hemodynamic instability and target organs damage and usually receive late reperfusion. Additional meta-analysis of 19 studies that included 6000 patients with STEMI showed similar benefit between thrombolysis and primary angioplasty (PCI) in diabetic and nondiabetic patients.⁷ In the same study, however the rates of recurrence myocardial infarction and stroke was lower in patients after primary angioplasty and additional patients with DM showed delayed onset of reperfusion and longer ischemic time and they have a significant delay in starting treatment due to atypical symptoms.

In Europe, 20–30% of patients with myocardial infarction without ST segment elevation (NSTEMACS) have known DM while a similar percentage is either undiagnosed diabetic patients or they have impaired glucose tolerance.^{5,8} An analysis of 15,000 patients with NSTEMACS diabetic patients was independently associated with increased 30-day and annual mortality.⁹ In addition diabetic NSTEMACS patients, usually are older, more often have pre-existing

cardiovascular disease, hypertension, and renal failure and have more often atypical symptoms.¹⁰ During hospitalization patients with DM are more likely to develop complications such as heart failure, stroke, recurrent myocardial infarction, renal failure and major bleeding.^{10,11}

From therapeutic view diabetic patients compared with nondiabetic patients, show decreased antiplatelet response to clopidogrel and aspirin and less favorable results after interventional (PCI) and surgical revascularization (CABG).^{12,13}

Specifically reperfusion therapy in diabetic patients with multivessel disease and NSTEMACS remains unclear due to lack of randomized studies comparing different strategies. The best results were obtained by comparing PCI and CABG in patients with multivessel stable coronary disease.^{14–16} Selection of reperfusion strategy in diabetic patients would be based on many factors such as clinical status evaluation (hemodynamic/electrical instability, ongoing ischemia), complex coronary artery disease, suitability of lesions for PCI and distal anastomoses in CABG, ischemic load, echocardiographic assessment of left ventricular function and any other comorbidities. Furthermore various scores of coronary lesions evaluation and predicting surgical mortality as SYNTAX, EuroSCORE II, STS should be taking in mind for decision making.¹⁷ The Heart Team is really important and all patients with DM and multivessel complex coronary artery disease should be evaluated.¹⁸ Overall the surgical reperfusion threshold compared with PCI in diabetic patients should be lower compared to non-diabetic patients and low-risk patients with multivessel coronary artery disease.^{14–16} In diabetic patients with ongoing ischemia or hemodynamic instability direct coronary angiography is appropriate and adequate reperfusion therapy must be selected individually and after discussion with the Heart Team understanding the increased risk of surgical reperfusion in continuing ischemia. Finally DES stents have dramatically reduced the need for repeat revascularization in diabetic patients and are suggested as first choice.¹⁹

Regarding antiplatelet therapy both diabetic and non-diabetic patients should be treated with the same drugs

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and the same dosages. Newer P2Y₁₂ inhibitors prasugrel and ticagrelor seem superior compared with clopidogrel in diabetic patients with ACS in the TRITON-TIMI 38 studies and PLATO.^{20,21} Corresponding GPIIb/IIIa inhibitors shown reduced mortality in diabetic patients with NSTEMI in pre clopidogrel time but their role now should be more elucidated.²² Despite the increased risk, antiplatelets such as thienopyridines are used less often in patients with diabetes than non-diabetic ones with an adverse effect on both the hospital and the long lasting mortality.^{6,23,24}

Important is the close follow up for contrast nephropathy of diabetic patients after PCI. Insufficient data exist to discontinue metformin 24–48 hours before angiography or PCI as the risk of lactic acidosis is negligible. Renal function should however be monitored after angioplasty in these patients.²⁵ In addition, as a general rule, less strict glucose control should be applied in patients with more advanced cardiovascular disease, older age, longer diabetes and more co-morbidities in acute phase and ACS follow up.

In conclusion DM increases the mortality of patients with ACS with many ways while the implementation of the appropriate therapeutic reperfusion intervention to whom and when require more randomized trials.

References

- van Dieren S, Beulens JW, van der Schouw YT, Grobbee DE, Neal B. The global burden of diabetes and its complications: an emerging pandemic. *Eur J Cardiovasc Prev Rehabil Off J Eur Soc Cardiol Work Groups Epidemiol Prev Cardiac Rehabil Exerc Physiol*. May 2010;17(suppl 1):S3–S8.
- Tillin T, Hughes AD, Mayet J, et al. The relationship between metabolic risk factors and incident cardiovascular disease in Europeans, South Asians, and African Caribbeans: SABRE (Southall and Brent Revisited) – a prospective population-based study. *J Am Coll Cardiol*. Apr 30 2013;61(17):1777–1786.
- Arnold SV, Lipska KJ, Li Y, et al. Prevalence of glucose abnormalities among patients presenting with an acute myocardial infarction. *Am Heart J*. Oct 2014;168(4), 466–470 e461.
- O'Donoghue ML, Vaidya A, Afsal R, et al. An invasive or conservative strategy in patients with diabetes mellitus and non-ST-segment elevation acute coronary syndromes: a collaborative meta-analysis of randomized trials. *J Am Coll Cardiol*. Jul 10 2012;60(2):106–111.
- Giraldez RR, Clare RM, Lopes RD, et al. Prevalence and clinical outcomes of undiagnosed diabetes mellitus and prediabetes among patients with high-risk non-ST-segment elevation acute coronary syndrome. *Am Heart J*. Jun 2013;165(6), 918–925 e912.
- Malmberg K, Yusuf S, Gerstein HC, 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*. Aug 29 2000;102(9):1014–1019.
- Scirica BM, Bhatt DL, Braunwald E, et al. Saxagliptin and cardiovascular outcomes in patients with type 2 diabetes mellitus. *N Engl J Med*. Oct 03 2013;369(14):1317–1326.
- Norhammar A, Tenerz A, Nilsson G, et al. Glucose metabolism in patients with acute myocardial infarction and no previous diagnosis of diabetes mellitus: a prospective study. *Lancet*. Jun 22 2002;359(9324):2140–2144.
- Donahoe SM, Stewart GC, McCabe CH, et al. Diabetes and mortality following acute coronary syndromes. *Jama*. Aug 15 2007;298(7):765–775.
- Dotevall A, Hasdai D, Wallentin L, Battler A, Rosengren A. Diabetes mellitus: clinical presentation and outcome in men and women with acute coronary syndromes. Data from the Euro Heart Survey ACS. *Diabet Med J Br Diabet Assoc*. Nov 2005;22(11):1542–1550.
- Subherwal S, Bach RG, Chen AY, et al. Baseline risk of major bleeding in non-ST-segment-elevation myocardial infarction: the CRUSADE (Can Rapid risk stratification of Unstable angina patients Suppress Adverse outcomes with Early implementation of the ACC/AHA Guidelines) bleeding score. *Circulation*. Apr 14 2009;119(14):1873–1882.
- Angiolillo DJ. Antiplatelet therapy in diabetes: efficacy and limitations of current treatment strategies and future directions. *Diabetes Care*. Apr 2009;32(4):531–540.
- Ferreiro JL, Angiolillo DJ. Diabetes and antiplatelet therapy in acute coronary syndrome. *Circulation*. Feb 22 2011;123(7):798–813.
- Kappetein AP, Head SJ, Morice MC, et al. Treatment of complex coronary artery disease in patients with diabetes: 5-year results comparing outcomes of bypass surgery and percutaneous coronary intervention in the SYNTAX trial. *Eur J Cardiothoracic Surg Off J Eur Assoc Cardio Thorac Surg*. May 2013;43(5):1006–1013.
- Kapur A, Hall RJ, Malik IS, et al. Randomized comparison of percutaneous coronary intervention with coronary artery bypass grafting in diabetic patients. 1-year results of the CARDia (Coronary Artery Revascularization in Diabetes) trial. *J Am Coll Cardiol*. Feb 02 2010;55(5):432–440.
- Farkouh ME, Domanski M, Sleeper LA, et al. Strategies for multivessel revascularization in patients with diabetes. *N Engl J Med*. Dec 20 2012;367(25):2375–2384.
- Roffi M, Angiolillo DJ, Kappetein AP. Current concepts on coronary revascularization in diabetic patients. *Eur Heart J*. Nov 2011;32(22):2748–2757.
- Windecker S, Kolh P, Alfonso F, et al. 2014 ESC/EACTS guidelines on myocardial revascularization: the task force on myocardial revascularization of the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS) developed with the special contribution of the European Association of Percutaneous Cardiovascular Interventions (EAPCI). *Eur Heart J*. Oct 01 2014;35(37):2541–2619.
- Bangalore S, Kumar S, Fusaro M, et al. Outcomes with various drug eluting or bare metal stents in patients with diabetes mellitus: mixed treatment comparison analysis of 22,844 patient years of follow-up from randomised trials. *BMJ*. Aug 10 2012;345:e5170.
- Wiviott SD, Braunwald E, Angiolillo DJ, et al. Greater clinical benefit of more intensive oral antiplatelet therapy with prasugrel in patients with diabetes mellitus in the trial to assess improvement in therapeutic outcomes by optimizing platelet inhibition with prasugrel-thrombolysis in myocardial infarction 38. *Circulation*. Oct 14 2008;118(16):1626–1636.
- James S, Angiolillo DJ, Cornel JH, et al. Ticagrelor vs. clopidogrel in patients with acute coronary syndromes and diabetes: a substudy from the PLATElet inhibition and patient Outcomes (PLATO) trial. *Eur Heart J*. Dec 2010;31(24):3006–3016.
- Roffi M, Chew DP, Mukherjee D, et al. Platelet glycoprotein IIb/IIIa inhibitors reduce mortality in diabetic patients with non-ST-segment-elevation acute coronary syndromes. *Circulation*. Dec 04 2001;104(23):2767–2771.
- Mehta SR, Granger CB, Eikelboom JW, et al. Efficacy and safety of fondaparinux versus enoxaparin in patients with acute coronary syndromes undergoing percutaneous coronary intervention: results from the OASIS-5 trial. *J Am Coll Cardiol*. Oct 30 2007;50(18):1742–1751.
- Wallentin L, Becker RC, Budaj A, et al. Ticagrelor versus clopidogrel in patients with acute coronary syndromes. *N Engl J Med*. Sep 10 2009;361(11):1045–1057.

25. Roffi M, Patrono C, Collet JP, et al. 2015 ESC guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation: task force for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation of the European Society of Cardiology (ESC). *Eur Heart J*. Jan 14 2016;37(3):267–315.

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