Journal of Diabetes and Its Complications 33 (2019) 465–467

Contents lists available at ScienceDirect

Journal of Diabetes and Its Complications

journal homepage: WWW.JDCJOURNAL.COM

Management of patients with type 2 diabetes mellitus and acute coronary syndrome: Better be safe than sorry!

Niki Katsiki [a,*], Dimitri P. Mikhailidis [b]

[a] First Department of Internal Medicine, Diabetes Center, Division of Endocrinology and Metabolism, Medical School, Aristotle University of Thessaloniki, AHEPA Hospital, Thessaloniki, Greece
[b] Department of Clinical Biochemistry, Royal Free Campus, University College London Medical School, University College London (UCL), London, UK

ARTICLE INFO

Article history:
Received 12 April 2019
Received in revised form 15 April 2019
Accepted 15 April 2019
Available online 25 April 2019

Keywords:
Type 2 diabetes mellitus
Acute coronary syndrome
Empagliflozin
Liraglutide
Dulaglutide
Statins

The prevalence of type 2 diabetes mellitus (T2DM) in acute coronary syndrome (ACS) patients (ranging from 20 to 40%) is increasing, following the T2DM epidemic and the improved survival of T2DM patients.[1,2] T2DM has been linked both to an increased ACS incidence and mortality.[3] Furthermore, T2DM significantly raises the risk for future major adverse cardiac events in ACS patients.[4] Hyperglycemia during hospitalization for ACS is recognized as a strong predictor of worse outcomes, even in the absence of DM.[5] Of note, undiagnosed T2DM patients may present with an ACS; the role of cardiologists, being aware of the increased prevalence of T2DM in the setting of an ACS, is important to ensure early T2DM diagnosis in these very-high risk patients.

Several mechanisms may be involved in the association between T2DM and ACS morbidity and mortality, including hyperglycemia-induced cardiac myocyte death and vascular damage via the protein kinase C, the advanced glycation end products, the polyol and the hexosamine pathways, as well as oxidative stress, inflammation, endothelial and platelet activation.[3,5] These pathophysiological processes can impair left ventricular function and cardiac perfusion, as well as promote thrombosis, thus predisposing to myocardial ischemia and decreased myocardial performance.[6]

In patients with non-ST segment elevation myocardial infarction (NSTEMI), coronary angiography and revascularization are recommended in the presence of T2DM.[7] In these patients, if there is stabilized multivessel disease and an acceptable surgical risk exists, coronary artery bypass grafting (CABG) is recommended over percutaneous coronary intervention (PCI).[7] In cases when PCI is performed, new-generation drug-eluting stents are preferred over bare-metal stents.[7]

With regard to glycemic control, insulin is the treatment of choice during hospitalization for ACS, initially administered intravenously and then subcutaneously when the acute critical phase of the ACS resolves.[2,5] In the long-term, since glycated hemoglobin A_{1c} is positively related to all-cause mortality, optimal glycemic control should be attained to improve survival.[2,8] In this context, and according to current (2019) guidelines, T2DM patients with a history of ACS should be treated, apart from metformin, with antidiabetic drugs with proven cardiovascular (CV) benefits, i.e. sodium-glucose co-transporter 2 (SGLT2i) or glucagon-like peptide-1 receptor agonist (GLP-1 RA).[9] Among SGLT2i, empagliflozin was shown to decrease the composite of MI, stroke and CV mortality, as well as hospitalization for heart failure (HF) in T2DM patients with established CV disease in the Empagliflozin Cardiovascular Outcome Event Trial in Type 2 Diabetes Mellitus Patients (EMPAREG-OUTCOME) ($n = 7020$).[10] Similar results were observed with canagliflozin in the Canagliflozin Cardiovascular Assessment Study (CANVAS) trials in T2DM patients ($n = 10{,}142$) with established CV disease (65.6%) or multiple CV risk factors.[11] Current guidelines mention that evidence is modestly stronger for empagliflozin than canagliflozin.[9] Furthermore, only empagliflozin significantly reduced CV and all-cause death,[10] whereas canagliflozin led to a doubled risk of amputations and an increased risk of fractures,[11] thus limiting its clinical use. These adverse events were not observed with empagliflozin treatment.[10,12]

Although not included in the guidelines,[9] dapagliflozin was shown to significantly decrease HF hospitalization in T2DM patients ($n = 17{,}160$) with established CV disease or multiple CV risk factors (59.4%) in the Dapagliflozin Effect on Cardio-vascular Events-Thrombolysis in Myocardial Infarction 58 (DECLARE-TIMI 58).[13] The composite endpoint of MI, stroke and CV death, as well as all-cause and CV mortality did not differ between dapagliflozin and placebo groups in patients with established CV disease or multiple risk factors.[13] No safety issues in terms of amputations and fractures were observed with dapagliflozin.[13] Thus, SGLT2i-induced risk of amputations may only be related to canagliflozin use and not to empagliflozin or dapagliflozin.[14] Of note, in a subanalysis of the DECLARE-TIMI 58 trial, dapagliflozin was shown to significantly

Declaration of interest: NK has given talks, attended conferences and participated in trials sponsored by Amgen, Angelini, Astra Zeneca, Boehringer Ingelheim, Mylan, Novo Nordisk, Sanofi and Servier. DPM has given talks and attended conferences sponsored by MSD, AstraZeneca and Libytec.

* Corresponding author at: First Department of Internal Medicine, AHEPA University Hospital, 1st Stilponos Kyriakidi Street, 546 21 Thessaloniki, Greece.
E-mail address: nikikatsiki@hotmail.com (N. Katsiki).

https://doi.org/10.1016/j.jdiacomp.2019.04.011

decrease the primary endpoint of CV death, MI or ischemic stroke in patients with prior MI (but not in those without a history of MI).[15] This benefit was mainly driven by reductions in the rates of recurrent MI, whereas stroke and CV mortality (as well as CHD and all-cause death) did not significantly differ between the dapagliflozin and placebo group. In another subanalysis of this study, dapagliflozin significantly decreased HF hospitalization in patients with and without HF with reduced ejection fraction (HFrEF); CV and total mortality were reduced only in patients with HFrEF.[16] It should be noted that, in the EMPAREG-OUTCOME trial, empagliflozin decreased HF hospitalization and CV mortality consistently in patients with and without HF at baseline.[17] Similarly, the reductions in the rates of the 3-point major adverse cardiac events (MACE) (i.e. MI, stroke and CV death), HF hospitalization, CV and all-cause mortality were consistent in patients with and without a prior stroke, MI, peripheral artery disease (PAD) or CABG.[18–20] Furthermore, empagliflozin-induced decrease in CV death was consistent across different types of CV disease (i.e. single and multivessel coronary artery disease, stroke, HF, PAD, MI, atrial fibrillation and CABG).[21] Interestingly, in the EMPAREG-OUTCOME trial, T2DM patients with left ventricular hypertrophy (LVH) benefited significantly more in terms of the 3-point MACE compared with those without LVH, whereas reductions in CV and all-cause mortality were similar, irrespective of the presence or absence of LVH at baseline.[22] A small ($n = 20$ T2DM patients, 24% had known CV disease) recent study reported that LV end diastolic volume (assessed by magnetic resonance imaging) was significantly decreased by empagliflozin at 6 months.[23] A previous study ($n = 10$ T2DM patients with known CV disease) showed that empagliflozin significantly reduced LV mass index at 3 months.[24] According to these findings, empagliflozin seems to be able to also affect cardiac remodeling.

Among GLP-1 RAs, only liraglutide, semaglutide and albiglutide were reported to significantly reduce the composite of CV morbidity and mortality (but not HF hospitalization) in the Liraglutide Effect and Action in Diabetes: Evaluation of Cardiovascular Outcome Results (LEADER),[25] the Trial to Evaluate Cardiovascular and Other Long-term Outcomes with Semaglutide in Subjects with Type 2 Diabetes (SUSTAIN-6)[26] and the Albiglutide and cardiovascular outcomes in patients with type 2 diabetes and cardiovascular disease (HARMONY) trials,[27] respectively. These CV benefits were largely driven by significant reductions in CV and total mortality for liraglutide, stroke for semaglutide and myocardial infarction (MI) for albiglutide. Of note, the CV effects of lixisenatide (a GLP-1 RA) and alogliptin (a dipeptidyl peptidase-4 inhibitor) were evaluated in T2DM patients post-ACS (within the previous 180 and 15–90 days, respectively) in the Evaluation of Lixisenatide in Acute Coronary Syndrome (ELIXA)[28] and the Examination of Cardiovascular Outcomes with Alogliptin versus Standard of Care (EXAMINE) trials,[29] respectively, with neutral results.

Overall, the majority of the abovementioned CV outcome trials with SGLT2i or GLP-1 RA (such as the EMPAREG-OUTCOME[10], CANVAS[11], DECLARE-TIMI 58[13], LEADER[25], SUSTAIN-6[26] and HARMONY[27] trials) did not involve ACS patients. Only the ELIXA[28] and the EXAMINE[29] trials included post-ACS T2DM patients, reporting no CV benefits. Furthermore, as mentioned previously, insulin is the treatment of choice during hospitalization for ACS; thus, SGLT2i or GLP-1 RA, as well as other oral antidiabetic drugs may be discontinued in T2DM patients that present with an ACS and replaced by insulin therapy during hospital stay. After discharge, empagliflozin should be preferably initiated, along with liraglutide, if needed (based on current guidelines[9] and since these drugs were shown to significantly improve outcomes and be safe).

Contrast-induced acute kidney injury (CI-AKI) could occur following coronary angiography/PCI, thus predisposing to prolonged hospital stay and increased CV and renal morbidity, as well as all-cause death, even in the long-term (data available up to 4 years).[30–34] Strategies preventing CI-AKI include hydration, antihypertensive drugs [loop diuretics, angiotensin-converting enzyme inhibitors (ACEi)], statins, adenosine antagonists, *N*-acetylcysteine, vitamin C, alprostadil and nicorandil.[35–38]

In T2DM patients already on metformin and SGLT2i, renal function should be carefully monitored for at least 3 days following coronary angiography/PCI).[39] If estimated glomerular filtration (eGFR) decreases to <45 ml/min per 1.73 m^2, treatment with SGLT2i should be discontinued and metformin should be given at a half dose (and discontinued if eGFR falls <30 ml/min per 1.73 m^2)). [9] After restoration of kidney function, metformin and SGLT2i could be re-administered.

With regard to antiplatelet drugs, more potent $P2Y_{12}$ receptor antagonists (i.e. prasugrel or ticagrelor) are preferred compared with clopidogrel in T2DM patients, since they exert higher absolute risk reductions in these patients).[39] In this context, current (2019) guidelines recommend the use of a P2Y12 receptor antagonist (ticagrelor, if PCI is not performed, ticagrelor or prasugrel if PCI is performed) combined with aspirin for at least 12 months following an ACS in T2DM patients.[9] In this context, a recent meta-analysis showed that ticagrelor and prasugrel exerted similar efficacy and safety in T2DM patients undergoing PCI.[40] However, in a substudy of the REgistry of New Antiplatelets in patients with Myocardial Infarction (RENAMI), ticagrelor therapy was related to significantly lower risks of total mortality and bleeding compared with prasugrel in T2DM patients after an ACS).[41]

Current guidelines recommend that a lipid profile is obtained as soon as possible in all patients, including those with T2DM, presenting with an ACS such as a ST-segment elevation MI (STEMI)). [39] High-intensity statin therapy (i.e. rosuvastatin 20–40 mg or atorvastatin 40–80 mg) should be initiated as early as possible and maintained thereafter).[42] In these patients, the low-density lipoprotein cholesterol (LDL-C) goal is <70 mg/dl or a 50% (at least) reduction if baseline LDL-C is between 70 and 135 mg/dl according to the European Society of Cardiology (ESC) guidelines.[39] The American Diabetes Association (ADA) also recommends the use of a high-intensity statin in T2DM patients with established CV disease).[9] Of note, the American Association of Clinical Endocrinologists (AACE) suggests that LDL-C target should be <55 mg/dl in patients at extreme CV risk such as those with T2DM and established CV disease[43].

Both the ESC and ADA recommend that, if LDL-C remains ≥70 mg/dl, despite maximally tolerated statin therapy, ezetimibe or a proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitor should be added.[9] In this context, ezetimibe added to simvastatin was shown to significantly reduce the primary endpoint of CV death, nonfatal MI, nonfatal stroke, unstable angina requiring rehospitalization and coronary revascularization (≥30 days after randomization) compared with simvastatin monotherapy in patients after an ACS in the Improved Reduction of Outcomes: Vytorin Efficacy International Trial (IMPROVE-IT).[44] This benefit (median follow-up 6 years) was mainly attributed to significant decreases in the rates of any MI and ischemic stroke. A secondary analysis of the IMPROVE-IT trial showed that these CV benefits were consistent in patients with and without T2DM and/or polyvascular disease, with even greater absolute risk reductions in these subgroups of patients.[45]

Evolocumab and alirocumab are the 2 commercially available proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitors. Evolocumab significantly lowered the risk of the composite of CV mortality, MI or stroke (± coronary revascularization or hospitalization for unstable angina) in statin-treated patients with established CV disease in the Further Cardiovascular Outcomes Research with PCSK9 Inhibition in Subjects with Elevated Risk (FOURIER) trial.[46] A prespecified analysis of the FOURIER trial showed that these benefits were consistent in patients with and without T2DM.[47] Similarly, alirocumab significantly lowered the risk of MI, stroke, CV mortality or unstable angina requiring hospitalization in patients with an ACS in the ODYSSEY trial, especially those with baseline LDL-C ≥100 mg/dl.[48] All-cause death was also significantly decreased by alirocumab. These results were consistent in all prespecified subgroup analyses.

According to current ESC guidelines, it is recommended that therapy with angiotensin converting enzyme inhibitor (ACEi) should be initiated in T2DM patients within 24 h of a STEMI.[39] If patients are intolerant to ACEi, angiotensin II receptor blockers (ARBs) should be administered,

preferably valsartan. Beta-blockers should be given to all patients following a STEMI, whereas mineralocorticoid receptor antagonists are recommended in those with left ventricular ejection fraction ≤40% and heart failure (HF) or T2DM already taking ACEi and beta-blockers (provided there are no contra-indications, such as renal failure or hyperkalemia).[39] Early initiation of beta-blockers is also recommended in patients with non-STEMI (NSTEMI) and ongoing ischemic symptoms.[7]

Overall, T2DM patients with ACS are at an increased CV risk and should be adequately treated with antidiabetic, antiplatelet, hypolipidemic and antihypertensive drugs. Lifestyle interventions, including smoking cessation, diet and physical exercise, should also be implemented in ACS patients with or without T2DM to maximize CV risk reduction.[39]

References

1. Norhammar A, Mellbin L, Cosentino F. Diabetes: prevalence, prognosis and management of a potent cardiovascular risk factor. Eur J Prev Cardiol 2017;24:52-60.
2. El Ouazzani J, Ghalem A, El Ouazzani G, Ismaili N, El Ouafi N. Management of hyperglycemia during and in the immediate follow-up of acute coronary syndrome. J Saudi Heart Assoc 2018;30:113-21.
3. Sasso FC, Rinaldi L, Lascar N, Marrone A, Pafundi PC, Adinolfi LE, et al. Role of tight glycemic control during acute coronary syndrome on CV outcome in type 2 diabetes. J Diabetes Res 2018;2018:3106056.
4. Chu CY, Lin TH, Lai WT. The management and prognostic factors of acute coronary syndrome: evidence from the Taiwan Acute Coronary Syndrome Full Spectrum Registry. Acta Cardiol Sin 2017;33:329-38.
5. Angeli F, Reboldi G, Poltronieri C, Aita A, Bartolini C, Verdecchia P. Detrimental effects of hyperglycemia in acute coronary syndromes: from pathophysiological mechanisms to therapeutic strategies. Mini Rev Med Chem 2015;15:1164-73.
6. Angeli F, Reboldi G, Poltronieri C, Lazzari L, Sordi M, Garofoli M, et al. Hyperglycemia in acute coronary syndromes: from mechanisms to prognostic implications. Ther Adv Cardiovasc Dis 2015;9:412-24.
7. Roffi M, Patrono C, Collet JP, Mueller C, Valgimigli M, Andreotti F, 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 2016;37:267-315.
8. Savonitto S, Morici N, Nozza A, Cosentino F, Perrone Filardi P, Murena E, et al. Predictors of mortality in hospital survivors with type 2 diabetes mellitus and acute coronary syndromes. Diab Vasc Dis Res 2018;15:14-23.
9. ADA. Pharmacologic approaches to glycemic treatment: standards of medical care in diabetes-2019. Diabetes Care 2019;42:S90-102.
10. Zinman B, Wanner C, Lachin JM, Fitchett D, Bluhmki E, Hantel S, et al. Empagliflozin, cardiovascular outcomes, and mortality in type 2 diabetes. N Engl J Med 2015;373:2117-28.
11. Neal B, Perkovic V, Mahaffey KW, de Zeeuw D, Fulcher G, Erondu N, et al. Canagliflozin and cardiovascular and renal events in type 2 diabetes. N Engl J Med 2017;377:644-57.
12. Inzucchi SE, Iliev H, Pfarr E, Zinman B. Empagliflozin and assessment of lower-limb amputations in the EMPA-REG OUTCOME trial. Diabetes Care 2018;41:e4-5.
13. Wiviott SD, Raz I, Bonaca MP, Mosenzon O, Kato ET, Cahn A, et al. Dapagliflozin and cardiovascular outcomes in type 2 diabetes. N Engl J Med 2019;380:347-57.
14. Katsiki N, Dimitriadis G, Hahalis G, Papanas N, Tentolouris N, Triposkiadis F, et al. Sodium-glucose co-transporter-2 inhibitors (SGLT2i) use and risk of amputation: an expert panel overview of the evidence. Metabolism 2019. [Epub ahead of print].
15. Furtado RHM, Bonaca MP, Raz I, Zelniker TA, Mosenzon O, Cahn A, et al. Dapagliflozin and cardiovascular outcomes in patients with type 2 diabetes and prior myocardial infarction: a sub-analysis from DECLARE TIMI-58 trial. Circulation 2019 Mar;18. [Epub ahead of print].
16. Kato ET, Silverman MG, Mosenzon O, Zelniker TA, Cahn A, Furtado RHM, et al. Effect of dapagliflozin on heart failure and mortality in type 2 diabetes mellitus. Circulation 2019 Mar;18. [Epub ahead of print].
17. Fitchett D, Zinman B, Wanner C, Lachin JM, Hantel S, Salsali A, et al. Heart failure outcomes with empagliflozin in patients with type 2 diabetes at high cardiovascular risk: results of the EMPA-REG OUTCOME® trial. Eur Heart J 2016;37:1526-34.
18. Fitchett D, Inzucchi SE, Cannon CP, McGuire DK, Scirica BM, Johansen OE, et al. Empagliflozin reduced mortality and hospitalization for heart failure across the spectrum of cardiovascular risk in the EMPA-REG OUTCOME trial. Circulation 2019;139:1384-95.
19. Verma S, Mazer CD, Al-Omran M, Inzucchi SE, Fitchett D, Hehnke U, et al. Cardiovascular outcomes and safety of empagliflozin in patients with type 2 diabetes mellitus and peripheral artery disease: a subanalysis of EMPA-REG OUTCOME. Circulation 2018;137:405-7.
20. Verma S, Mazer CD, Fitchett D, Inzucchi SE, Pfarr E, George JT, et al. Empagliflozin reduces cardiovascular events, mortality and renal events in participants with type 2 diabetes after coronary artery bypass graft surgery: subanalysis of the EMPA-REG OUTCOME® randomised trial. Diabetologia 2018;61:1712-23.
21. Fitchett D, Inzucchi SE, Lachin JM, Wanner C, van de Borne P, Mattheus M, et al. Cardiovascular mortality reduction with empagliflozin in patients with type 2 diabetes and cardiovascular disease. J Am Coll Cardiol 2018;71:364-7.
22. Verma S, Mazer CD, Bhatt DL, Raj SR, Yan AT, Verma A, et al. Empagliflozin and cardiovascular outcomes in patients with type 2 diabetes and left ventricular hypertrophy: a subanalysis of the EMPA-REG OUTCOME trial. Diabetes Care 2019;42:e42-4.
23. Cohen ND, Gutman SJ, Briganti EM, Taylor AJ. The effects of empagliflozin treatment on cardiac function and structure in patients with type 2 diabetes - a cardiac MR study. Intern Med J 2019 Feb;19. [Epub ahead of print].
24. Verma S, Garg A, Yan AT, Gupta AK, Al-Omran M, Sabongui A, et al. Effect of empagliflozin on left ventricular mass and diastolic function in individuals with diabetes: an important clue to the EMPA-REG OUTCOME trial? Diabetes Care 2016;39:e212-3.
25. Marso SP, Daniels GH, Brown-Frandsen K, Kristensen P, Mann JF, Nauck MA, et al. Liraglutide and cardiovascular outcomes in type 2 diabetes. N Engl J Med 2016;375:311-22.
26. Marso SP, Bain SC, Consoli A, Eliaschewitz FG, Jódar E, Leiter LA, et al. Semaglutide and cardiovascular outcomes in patients with type 2 diabetes. N Engl J Med 2016;375:1834-44.
27. Hernandez AF, Green JB, Janmohamed S, D'Agostino Sr RB, Granger CB, Jones NP, et al. Albiglutide and cardiovascular outcomes in patients with type 2 diabetes and cardiovascular disease (Harmony Outcomes): a double-blind, randomised placebo-controlled trial. Lancet 2018;392:1519-29.
28. Pfeffer MA, Claggett B, Diaz R, Dickstein K, Gerstein HC, Køber LV, et al. Lixisenatide in patients with type 2 diabetes and acute coronary syndrome. N Engl J Med 2015;373:2247-57.
29. White WB, Cannon CP, Heller SR, Nissen SE, Bergenstal RM, Bakris GL, et al. Alogliptin after acute coronary syndrome in patients with type 2 diabetes. N Engl J Med 2013;369:1327-35.
30. Katsiki N, Fonseca V, Mikhailidis DP. Contrast-induced acute kidney injury in diabetes mellitus: clinical relevance and predisposing factors. Could statins be of benefit? J Diabetes Complications 2018;32:982-4.
31. Sun G, Chen P, Wang K, Li H, Chen S, Liu J, et al. Contrast-induced nephropathy and long-term mortality after percutaneous coronary intervention in patients with acute myocardial infarction. Angiology 2018 Oct 15. [Epub ahead of print].
32. Uzunhasan I, Yildiz A, Arslan S, Abaci O, Kocas C, Kocas BB, et al. Contrast-induced acute kidney injury is associated with long-term adverse events in patients with acute coronary syndrome. Angiology 2017;68:621-6.
33. Katsiki N, Tsioufis C, Hahalis G, Athyros VG. Contrast-induced acute kidney injury: beware of the risk after coronary angiography. Expert Rev Cardiovasc Ther 2018;16:73.
34. Katsiki N, Athyros VG, Karagiannis A, Mikhailidis DP. Contrast-induced nephropathy: an "all or none" phenomenon? Angiology 2015;66:508-13.
35. Yang SC, Fu NK, Zhang J, Liang M, Cong HL, Lin WH, et al. Preventive effects of alprostadil against contrast-induced nephropathy inpatients with renal insufficiency undergoing percutaneous coronary intervention. Angiology 2018;69:393-9.
36. Zhan B, Huang X, Jiang L, Bao H, Cheng X. Effect of nicorandil administration on preventing contrast-induced nephropathy: a meta-analysis. Angiology 2018;69:568-73.
37. Mikhailidis DP, Athyros VG. Acute kidney injury: short-term statin therapy for prevention of contrast-induced AKI. Nat Rev Nephrol 2014;10:8-9.
38. Ali-Hasan-Al-Saegh S, Mirhosseini SJ, Ghodratipour Z, Sarrafan-Chaharsoughi Z, Rahimizadeh E, Karimi-Bondarabadi AA, et al. Strategies preventing contrast-induced nephropathy after coronary angiography: a comprehensive meta-analysis and systematic review of 125 randomized controlled trials. Angiology 2017;68:389-413.
39. Ibánez B, James S, Agewall S, Antunes MJ, Bucciarelli-Ducci C, Bueno H, et al. 2017 ESC guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation. Rev Esp Cardiol (Engl Ed) 2017;70:1082.
40. Yang H, Tang B, Xu CH, Ahmed A. Ticagrelor versus prasugrel for the treatment of patients with type 2 diabetes mellitus following percutaneous coronary intervention: a systematic review and meta-analysis. Diabetes Ther 2019;10:81-93.
41. Conrotto F, Bertaina M, Raposeiras-Roubin S, Kinnaird T, Ariza-Solé A, Manzano-Fernández S, et al. Prasugrel or ticagrelor in patients with acute coronary syndrome and diabetes: a propensity matched substudy of RENAMI. Eur Heart J Acute Cardiovasc Care 2018 Oct 1. 2048872618802783 [Epub ahead of print].
42. Katsiki N, Triposkiadis F, Giannoukas AD, Mikhailidis DP. Statin loading in cardiovascular surgery: never too early to treat. Curr Opin Cardiol 2018;33:436-43.
43. Garber AJ, Abrahamson MJ, Barzilay JI, Blonde L, Bloomgarden ZT, Bush MA, et al. Consensus statement by the American association of clinical endocrinologists and American college of endocrinology on the comprehensive type 2 diabetes management algorithm-2018 executive summary. Endocr Pract 2018;24:91-120.
44. Cannon CP, Blazing MA, Giugliano RP, McCagg A, White JA, Theroux P, et al. Ezetimibe added to statin therapy after acute coronary syndromes. N Engl J Med 2015;372:2387-97.
45. Bonaca MP, Gutierrez JA, Cannon C, Giugliano R, Blazing M, Park JG, et al. Polyvascular disease, type 2 diabetes, and long-term vascular risk: a secondary analysis of the IMPROVE-IT trial. Lancet Diabetes Endocrinol 2018;6:934-43.
46. Sabatine MS, Giugliano RP, Keech AC, Honarpour N, Wiviott SD, Murphy SA, et al. Evolocumab and clinical outcomes in patients with cardiovascular disease. N Engl J Med 2017;376:1713-22.
47. Sabatine MS, Leiter LA, Wiviott SD, Giugliano RP, Deedwania P, De Ferrari GM, et al. Cardiovascular safety and efficacy of the PCSK9 inhibitor evolocumab in patients with and without diabetes and the effect of evolocumab on glycaemia and risk of new-onset diabetes: a prespecified analysis of the FOURIER randomised controlled trial. Lancet Diabetes Endocrinol 2017;5:941-50.
48. Schwartz GG, Steg PG, Szarek M, Bhatt DL, Bittner VA, Diaz R, et al. Alirocumab and cardiovascular outcomes after acute coronary syndrome. N Engl J Med 2018;379:2097-107.