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IMPLICATIONS OF DIABETES MELLITUS IN PATIENTS WITH ACUTE CORONARY SYNDROMES - POORER OUTCOMES AMONG DIABETICS

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Abstract
Cardiovascular disease is the leading cause of death in the world, causing over 17 million deaths annually, of which 7.2 million by coronary heart disease. They are a major public health problem worldwide, of which acute coronary syndromes show special attention due to increased prevalence and incidence and poor prognosis. Although advanced therapies can improve the morbidity and mortality associated with acute coronary syndromes in well-developed countries, developing countries remain exposed to the ravages of these diseases. Of the patients admitted for acute coronary syndrome, about 30% suffer from diabetes mellitus, considered a major risk factor and a predictor for unfavorable evolution regardless of the type of acute coronary syndrome.
Keywords: *diabetes mellitus, acute coronary sindrome, poorer outcomes, myocardial revascularization*

Rezumat
Bolile cardiovasculare reprezintă principala cauză de mortalitate în lume, provocând peste 17 milioane de decese anual, dintre care 7,2 milioane prin boli coronariene. Ele reprezintă o problemă de sănătate publică majoră la nivel mondial, dintre care sindroamele coronariene acute atrag o atenție deosebită ca urmare a prevalenței și incidenței în creștere și prognosticului precar. Deși terapiile avansate pot scădea morbiditatea și mortalitatea asociate sindroamelor coronariene acute în țările bine dezvoltate, țările în curs de dezvoltare rămân expuse ravagiilor acestor boli. Dintre pacienții internați pentru sindroam coronarian acut, aprox 30% suferă de diabet zaharat, considerat un factor de risc major și un predictor de evoluție nefavorabilă indiferent de tipul sindromului coronarian acut.
Cuvinte cheie: *diabet zaharat, sindrom coronarian acut, evoluție nefavorabilă, revascularizare miocardică*

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Diabetes mellitus is among the top five causes of death in developed countries, with an increasing prevalence and a projection of 333 to 472 million patients in 2025, and an increase of 522 million diabetic patients in 2030 is estimated. Epidemiological studies shows an increase in blood sugar levels in the general population as well as an increase in diabetes mortality. Also, the association of diabetes increases cardiovascular mortality despite the therapeutic advances over the past three decades.

Diabetes is an independent risk factor for the development of atherosclerotic coronary artery disease. The prevalence of coronary artery disease is approximately 50% in diabetic patients compared to 2-4% in the general population. Numerous studies have highlighted an increased incidence of bi and trivascular coronary artery disease in diabetic patients compared to nondiabetics. Also, main trunk damage is more common and severe among these patients.

Patients with DZ develop coronary artery disease at a younger age than non-diabetics and have a less favorable progression than these. Associated vegetative neuropathy is delaying hospital presentation and, thus, the initiation of specific treatment. In addition, arrhythmias, recurrent ischemia, reinfarction, and heart failure can often complicate the evolution of these patients. Multiple pathophysiological mechanisms accelerate the formation of the atheroma plaque and thrombosis, thus contributing to the occurrence of acute coronary syndromes. Diabetes mellitus can be defined as a syndrome that is based on hyperglycemia, associated with changes in protein and lipid metabolism.

Interrelation with the cardiovascular system is supported by various pathophysiological changes occurring in the diabetic patients. Insulin resistance results in stimulation of vascular cell growth and migration and the growth of adhesion molecules VCAM-1, E-selectin and PAI-1 by endothelial cells. The negative effects of hyperglycemia are manifested by nonenzymatic and enzymatic glycosylation of the proteins, and thus, increasing the serum level of VLDL and LDL lipoproteins, modifying the structure and function of proteins, thickening the basal membranes and the capillary walls. Also, the polyol pathway, with secondary nerve demyelinating, leads to the occurrence of diabetic neuropathy, translated from a cardiovascular point of view by tachycardia, QT prolongation, orthostatic hypotension and lack of pain in myocardial infarction. Glycosylation of proteins and hemoglobin leads haematological disorders characterized by procoagulant and prothrombotic status. Also, proinflammatory status accelerates the progression of atherosclerosis in diabetic patients.

Factors favoring myocardial infarction in diabetics

Myocardial infarction often involves the occlusion of the coronary vascular lumen by the thrombus formed at the level of the atheroma plaque as a result of its breakage. Progression of atherosclerosis can also be caused by repeated cycles of ruptures, thrombosis and healing resulting in narrowing the coronary lumen.

Accelerated atherosclerosis.

Increased serum lipid levels induce vascular lesions and favor atherogenesis. Morphopathological studies suggest that lipid-rich atherosclerotic plaques are more prone to rupture than fibrous plaques. Unlike nondiabetic patients, patients with diabetes seem to have a larger number of such plaques. Despite the prevalence of lipid abnormalities in patients with diabetes, the contribution of total cholesterol to the development of coronary artery disease is not as important as VLDL cholesterol and triglycerides. Thus, the lipid profile of diabetic patients defined by elevated serum levels of VLDL, LDL cholesterol and triglycerides is associated with an increased risk of developing atherosclerotic coronary artery disease.

Hyperinsulinemia

Hyperinsulinaemia, more common among non-insulin-requiring diabetic patients with insulin resistance, is a risk factor for atherogenesis. It causes the proliferation of vascular smooth muscle cells and increases endogenous cholesterol synthesis. Even in the presence of a normal glucose tolerance, hyperinsulinemia is a risk factor for coronary atherosclerosis. Hyperglycemia is a risk factor for atherosclerosis, but not an independent risk factor for coronary artery disease.

Hematological disorders

The formation of the potential occlusive thrombus of the coronary vessel occurs through a dynamic process that depends on the balance between coagulation factors and their opponents. In diabetic patients, abnormalities have been identified with respect to platelet function, coagulation, fibrinolysis, endothelial function. Platelet aggregation is an essential step in the process of forming the thrombus.

Spontaneous and induced platelet aggregation is favored by pathophysiological changes in diabetics, thereby increasing the risk of cardiovascular events. Diabetic platelets synthesize increased amounts of thromboxane A2 that favor aggregation and cause vascular spasm. Increased levels of thromboxane A2 have been identified in patients with uncontrolled glycemic or vascular complications. Also, two types of platelets, betatromboglobulin and platelet factor 4, were found in much higher levels among diabetics. Plasma fibrinogen is found in higher amounts, which correlate with increased risk of myocardial infarction and sudden death in diabetic men. Fibrinopeptide A reflects platelet activity and it is also find often in increased amounts.

Autonomous neuropathy

The development of symptomatic autonomic neuropathy among diabetics associates an increase in mortality up to 50% three years after occurrence. Sudden cardiac arrest is responsible for 33% of deaths. Parasympathetic heart nerve fibers are affected before the sympathetic ones, resulting in increased sympathetic tone, clinically manifested by resting tachycardia, and

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diminishing pressure and heart reaction at exercise. Parasympathetic heart nerve fibers can also be responsible for coronary vasoconstriction, which can determine or aggravate myocardial ischaemia. The main clinical manifestation of sympathetic dysfunction is orthostatic hypotension. Autonomous neuropathy can lead to myocardial ischemia through various pathways: increased oxygen demand due to tachycardia, reduced myocardial blood flow by increasing coronary tone, reduced coronary perfusion pressure during orthostatic hypotension, decreased early signs of ischemia. Additionally, autonomic neuropathy is also responsible for the sudden death of diabetics. Although sudden death may occur as a result of secondary arrhythmia of a clinically silent acute myocardial infarction, morphopathological studies have demonstrated that it can occur in diabetics without coronary artery disease. Instead, it has been shown in these patients the link between autonomic neuropathy and prolonged QT interval, predisposing to malignant cardiac arrhythmias that lead to sudden death.

Altered perception of ischemia

Diabetics have a reduced perception of pain caused by myocardial ischemia. As a result, myocardial ischemia or myocardial infarction may be associated with a reduced symptomatology or complete absence of symptoms, a condition found in about 50% of diabetics. Clinically silent myocardial infarction is more common in diabetics, a fact supported by morphopathological studies which showed that the presence of post-infarction myocardial scarring in deceased patients without a history of ischemic cardiopathy was 3 times more common in diabetics compared to non-diabetic patients. The perception of ischemic symptoms in diabetics are far more late than nondiabetics. The time from the onset of ST segment changes to the occurrence of ischemic symptoms may be double in these patients and correlates with the degree of autonomic nerve dysfunction. Deterioration of afferent nerve fibers responsable for the transmission of painful nerve impulses secondary to myocardial ischaemia is responsible for this delay in symptomatology. Thus, the intensity of painful symptoms or atypical symptoms frequently characterizes diabetic patients. Often, the clinical diagnosis of myocardial ischaemia is difficult. Atypical symptoms such as confusion, dyspnea, fatigue, symptoms of dyspeptic syndrome may be their main reason for presenting in the emergency room. The atypical clinical picture decreases the clinical suspicion of a myocardial infarction, prevents appropriate triage in the emergency service and delays the diagnosis.

Screening of coronary artery disease in diabetic patients

DM is considered as an equivalent risk of ischemic heart disease. Framingham has shown that a patient with type 2 diabetes has the same risk of myocardial infarction at 7 years as a patient with a history of myocardial infarction. Current guidelines for diabetes management and cardiovascular disease management continue to treat diabetes as an equivalent risk of cardiovascular disease or a very high risk when combined with pre-existing cardiac disease or injuries to other organs such as kidneys. The Cardiovascular Prevention Guide of Society European Cardiology in 2016 and the recommendations for the management of dyslipidemia of the International Atherosclerosis Society are such guides. Other recent guidelines (the European Association for the Study of Diabetes, the Canadian Diabetes Association, the International Diabetes Federation etc.) recommend the use of either non-specific or specific predictive cardiovascular risk scores.

Non-specific cardiovascular risk scoring systems are based on the reason that diabetes does not alter the effect of other cardiovascular risk factors. The recent equation proposed by the American Heart Association (ACC / AHA ASCVD Risk Calculator) considers diabetes as an independent risk factor without interactions with other risk factors. Thus, other risk factors such as systolic blood pressure or HDL levels will equally contribute to the risk of cardiovascular disease, regardless of the presence of diabetes. This was the basis for other risk scores, such as Framingham cardiovascular risk equations.The fundamental difference between the risk scores based on the above principle and the risk scores specific to patients with diabetes is the interaction between diabetes and other risk factors. Echouffo-Tcheugui and Kengne systematically analyzed 22 pair comparisons of these two types of risk scores, of which 14 comparisons showed higher statistics for diabetes-specific models such as UKPDS, ADVANCE or DCS than risk models for the general population. One study showed that the UKPDS score has a cardiovascular disease prediction index lower than the one developed by Joint British Societies (0.74 vs. 0.80) and CardioRisk Manager (0.65 vs. 0.77)

The pattern of coronary involvement

Vascular caliber

Coronary artery caliber is associated with the body mass index and tends to be lower in women. Angiographic studies have revealed a much smaller caliber in diabetic patients. This aspect draws multiple complications in the interventional treatment of patients with acute coronary syndrome, with a higher in-hospital mortality after coronary angioplasty. The risk of restenosis is much higher, which draws the need for repeated revascularization after PCI.

Number of vessels involved

The number of affected vessels predict the morbidity and cardiac mortality of diabetic patients. Diabetics, generally, have a higher incidence of multivascular disease. CONFIRM study, which evaluated diabetics coronary leasions using computed tomography, revealed a a 37% higher prevalence of obstructive lesions compared to non-diabetics and trivascular coronary disease (13.5% versus 9.25%) in these patients.

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Location of coronary artery leasions

Proximal and osteal lesions are prognostically significant and are associated with a lower procedural success rate and a higher rate of major adverse cardiac events after PCI. A higher incidence of these events was observed in multiple angiographic studies as well as the left main trunk involvement among these patients.

Types of lesions

The lesions located at the bifurcation of two epicardial vessels represent a challenge for the interventional cardiologist and involve an increased risk of major cardiovascular events. It is not known exactly the incidence of these lesions among diabetics, but a study conducted on diabetic patients requiring interventional treatment revealed a poorer outcome in patients with bifurcation coronary injuries compared to ostial and median third leasion as well as a higher incidence of cardiovascular events 2 years after PCI. Similarly, total coronary occlusions appear to be more common in diabetics and often with worse postangiophic result.

Collateral circulation

The development of collateral vessels is triggered by the pressure gradient between the obstructive artery and myocardial ischaemia. However, a poor development of collateral vessels in some patients, despite the presence of coronary obstruction and evidence of myocardial ischaemia, suggest that additional factors may contribute to collateral development. Limited data are available about the development of collateral circulation in diabetics. There has been an increased interest in the literature for the functional impact of DZ on coronary vascular function. High glucose concentration has been shown to cause endothelial dysfunction. Different clinical and morphopathological studies have shown that diabetes appears to be an inhibitor of coronary collagen development. Other studies have argued that although diabetes is known to affect the vascular system, these underlying metabolism anomalies do not inhibit the formation of collateral vessels because diabetes affects small arteries, and collateral vessels are usually large epicardial vessels that do not seem to be affected by diabetes. However, it should be taken into account that colaterals are small vessels at the beginning of angiogenesis.

Calcification of coronary arteries

The onset of coronary atherosclerosis is parallel to the development of their calcification. Both insulin resistance and noninsuline-induced diabetes mellitus are associated with elevated calcium score of the coronary arteries. Computed tomography (CT) imaging shows that individuals affected

by diabetes have extensive calcification of coronary arteries that reflect a risk of increased cardiovascular events. Thus, a higher calcium score in diabetes predicts mortality from all causes. In addition, percutaneous coronary angioplasty involving a calcified lesion is associated with a reduced procedural success risk and an increased risk of fatal cardiovascular events after PCI.

Therapeutic management

Although there have been considerable improvements in the management of patients with coronary artery disease, the risk of acute coronary events remains high among patients with diabetes. Therefore, optimal medical therapy and adequate selection of myocardial revascularization strategy is critical for diabetic patients. Currently, the efficacy of various medical therapies and revascularization strategies in patients is under constant debate.

Glycemic control

Strict glycemic control is associated with an increased risk of hypoglycemia and has no benefit to mortality. The ACCORD trial was designed to test whether glycemic control treatment reduces the risk of cardiovascular events in type 2 diabetes. More than ten thousand patients were randomized to either a strategy of standard treatment targeting HbA1c levels between 7% and 8%, or for an intensive strategy with a hemoglobin target under(Hb) A1c <6.0%. Median HbA1c with the standard strategy was 7.5% and the intensive strategy reached a median HbA1c of 6.4%. However, in February 2008, the ACCORD glycemic control study was stopped due to the finding of an increased mortality rate in the intensive arm compared to the standard arm (1.41 vs 1.14% per year, 257 versus 203 deaths over a medium period follow-up of 3.5 years risk ratio [HR] 1.22 [95% CI 1.01-1.46]).

Analyzing the possible causes of mortality in the ACCORD study (evaluation of variables, including weight gain, use of any combination of drugs or drugs and hypoglycaemia) could not identify an explanation of increased mortality in the intensive arm. In both arms, participants with severe hypoglycaemia had a higher mortality than those without severe hypoglycaemia. However, there was a complex interaction between hypoglycemia, the arm of study and mortality. Among the participants with at least one episode of severe hypoglycaemia, mortality was higher in those in the standard arm of treatment, while among participants without a history of severe hypoglycaemia, mortality was higher in the intensive arm.

The ADVANCE study randomized 11,140 participants from Europe, Australia / New Zealand, Canada and Asia for an intense glycemic control strategy (primary therapy being sulfonylurea gliclazide and additional medicines needed to reach an A1C target of ≤6.5%) or standard therapy (in which any drug except gliclazide could be used). Study participants were slightly older and with a cardiovascular risk similar to those of the ACCORD study. Median levels of Hb A1C obtained in the intensive and standard arms were 6.3 and 7.0%. Intensive glycemic control reduced microvascular complications (0.86 [0.77-0.97], P =0.01), but without similar effects on macrovascular complications (0.94 [0.84-1.06], P = 0.32). There was no increase in general or cardiovascular mortality in the intensive arm compared to standard glycemic control arms.

Another VADT study included 1791

participants with uncontrolled type 2 diabetes who underwent an intense glycemic control strategy (HbA1C objective <6.0%) or standard glycemic control. For an average follow-up period of 5.6 years, the incidence of cardiovascular events was not significantly lower in the intensive arm (HR 0.88 [95% CI 0.74-1.05], P =0.12). There were more cardiovascular deaths in the intensive arm than in the standard arm (38 vs 29, sudden deaths 11 vs. 4), but the difference was not statistically significant.

It is biologically plausible that severe hypoglycaemia may increase the risk of death in patients with high cardiovascular risk. There is a clear J-shaped relationship between blood glucose levels and cardiovascular mortality. Mechanisms through which hypoglycaemia may cause cardiovascular events include adrenal-sympathetic activation, abnormal cardiac repolarisation, accelerated thrombogenesis, inflammation and vasoconstriction leading to cardiac ischaemia or fatal arrhythmia during recognized or unrecognized hypoglycaemia.

Myocardial revascularization in patients with type 2 diabetes

Patients with diabetes and cardiovascular disease have a higher risk of cardiovascular events, regardless of symptoms. If a patient with stable ischemic heart disease should undergo prompt revascularization remains an important clinical issue with extensive implications on the risks and benefits of treatment.

Revascularization vs. Medical Therapy

In the diabetic subgroup of the COURAGE study, which included 33% of all randomized patients, no benefit of PCI over drug therapy was observed with regard to death from any cause or non-fatal myocardial infarction during 4.6 years of follow-up (risk ratio [HR], 0.99, 95% confidence interval [CI], 0.73-1.32).

In BPI 2D, 19 patients with PCI had similar rates of major adverse events as those treated with MT, including non-fatal MI (11.3% vs. 10.2%). Although BARI 2D was not designed to compare PCI with CABG, it was observed that patients treated with CABG showed significantly less major cardiac events than those treated with MT, a finding that was mainly determined by a reduction in non-fatal myocardial infarction cases (7.4% versus 14.6%).

PCI versus CABG

The Coronary Artery Revascularization in Diabetes trial was the first randomized trial of coronary revascularization in patients with

diabetes. The study results did not show significant superiority for CABG compared to PCI, however, the study was undermined for such a statement. This was also the case for VA CARDS (Coronary Artery Revascularization in Diabetes) which was prematurely stopped due to slow recruitment; no firm conclusion on the comparative efficacy of PCI and CABG was possible. The first study that clearly demonstrates that CABG should be the preferred strategy of revascularization in patients with diabetes and multivascular disease was the FREEDOM trial.

Bypass Angioplasty Revascularization Investigation (BARI) described a mortality rate 3 times higher 5 years after percutaneous transluminal coronary angioplasty rather than CABG (20.6% vs. 5.8%, P =0.0003). Other studies have suggested equivalent results, none suggested a survival advantage of PCI.

The SYNTAX (Synergy Between Percutaneous Coronary Intervention with Taxus and Cardiac Surgery) trial did not reveal a significant difference in PCI mortality compared to CABG in the diabetic subgroup after 5 years of follow-up (19.5% vs. 12.9%, P = 0.065).

Future Revascularization Evaluation in Patients with Diabetes Mellitus (FREEDOM) reported a higher risk of death, stroke or stroke after PCI than after CABG (26.6% vs. 18.7% P =0.005), which was determined by higher rates of MI (13.9% versus 6.0%, P <0.001) and death from any cause after 5 years of follow-up (16.3% vs. 11, 0%)

Indications of PCI in diabetics

For diabetic patients who remain symptomatic despite optimal drug therapy or who have severe coronary artery disease, percutaneous coronary angioplasty is indicated. In particular, diabetic patients with stable ischemic heart disease, focal lesions and a low SYNTAX score of ≤22, PCI may be an alternative to CABG, given the long-term favorable outcome and a lower risk of stroke after PCI than after CABG (2.4% vs 5.2%, P = 0.03), according to data reported in the SYNTAX trial. Diabetic patients with multivascular coronary artery disease and acute coronary syndrome refractory to drug therapy should benefit from PCI urgently to solve the culprit lesion. In the majority of diabetics with multivascular coronary artery disease, especially with proximal left coronary artery leasion , CABG is the preferred method of revascularization, based on evidence from clinical trials.

Diabetics with ST segment elevation MI have PCI indication for acute lesion resolution according to European guidelines for myocardial revascularization. If multivascular disease is descovered, after emergency coronary angioplasty, it will be decided if drug therapy, PcI or CAGB is best suited for solving outstanding lesions. If cardiogenic shock complicates ST segment elevation myocardial infarction, PCI is an option as long as CAGB can not be done urgently.

Outcomes after percutaneous coronary intervention in diabetics

In patients with type II diabetes, coronary artery disease tends to be more complex, with multivascular, diffuse, calcific involvement, and often requires coronary revascularization in addition to optimal drug therapy for angina control. With regard to coronary revascularization, recent advances in techniques and devices used during percutaneous coronary intervention (PCI) have expanded the indication of PCI to more

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complex lesions. In particular, pharmacologically active stents (DES) reduced the rate of coronary restenosis and revascularization. However, the morbidity and mortality of diabetic patients with coronary artery disease continues to be high, even in the current era of drug eluting stents.

The need for repeated revascularisation and the mortality rate after PCI in diabetic patients are mediated by two important processes: restenosis and progression of coronary artery disease. These processes are secondary to metabolic disorder resulting from chronic hyperglycemia and insulin resistance. Diabetes mellitus is associated with platelet and endothelial dysfunction that is validated by accelerated atherosclerosis and atherosclerotic plaque instability. Atheromatous plaques formed in diabetic patients have a high content of lipids and phagocytes. This composition gives them an unstable character with ulceration and thrombus formation at this level. Thus, diabetic patients with acute coronary syndrome are more susceptible to extensive atheromatous lesions associated with ulceration and intracoronary thrombus. Endothelial dysfunction is supposed to induce negative arterial remodeling in response to atherosclerosis, resulting in lumen narrowing.

In-stent restenosis is caused by neointimal proliferation of vascular smooth muscle cells as a consequence of endothelial damage after balloon dilation and stent placement. Restenosis and mortality rates are significantly higher in diabetic patients after PCI. Almost all trials involving diabetes patients, including the FREEDOM trials at one year, reported higher rates of revascularisation after PCI than after CABG (12.6% vs. 4.8%, P <0.001). Also, as in FREEDOM (13.9% versus 6.0%, P <0.001), most studies in diabetic patients reported higher rates of myocardial infarction after PCI than after CABG.A distinctive sign of diabetic arteriopathy is medial calcification. Although it is difficult to quantify angiographically, coronary calcification can be associated with suboptimal results after PCI. A recent study however suggested that diabetes alone (HR, 2.10; 95% CI, 1.56-2.83) was a strong independent predictor of all-cause mortality at 1 year after PCI than calcification of the lesion (HR, 1.10, CI 95% 0.81-1.48).

A major progress in interventional cardiology were the new generations of pharmacologically active stents. In the FREEDOM study, almost all patients in the PCI group were treated with first-generation DESs that in current practice are replaced by more recent DESs. The new generation of pharmacologically active stents overcame the critical problem of intrastent thrombosis, various meta-analyzes showing that the everolimus stent (EES) reduced myocardial

infarction and intrastent thrombosis compared to other DESs. Bangalore et al. Reported that survival after implantation of pharmacological stents with everolimus is no different from CABG in diabetic patients with multivascular disease. The EXCEL trial claims that for the treatment of patients with coronary artery disease and low or intermediate SYNTAX scores, Everolimus elution stent PCI was not inferior to CABG in terms of risk of death, stroke or myocardial infarction 3 years of follow-up. BEST trial, however, points out that among patients with multivascular coronary artery disease, the rate of major adverse cardiovascular events was higher among those who underwent percutaneous angioplasty using everolimus stents than among those who underwent surgical revascularization.

Studies at the molecular, cellular and clinical levels agree that diabetic coronary disease is more aggressive. Understanding these differences and developing treatment interventions based on these observations are essential for improving PCI outcomes in these patients. Although most clinical trials in diabetic patients with coronary artery disease have revealed the superiority of CABG versus PCI in terms of repeated revascularization and incidence of myocardial infarction and mortality, it is not feasible to perform surgical revascularization in all diabetic patients with multivascular coronary artery disease. The surgical revascularization procedure is invasive in contrast to PCI, the choice of such a therapy depends not only on the complexity of the lesion, but also on the medical history and the patient's comorbidities. For the choice of the optimal therapeutic option, various intraoperative risk scores are useful, such as SYNTAX SCORE that establishes accurate mortality predictions to guide the choice between PCI and CABG for patients with multivascular coronary artery disease. EuroSCORE is also a useful scoring system that relies on the basic clinical information of a patient that could predict intraoperative mortality for patients undergoing cardiac surgery.

References

1. Cardiovascular risk and diabetes. Are the methods of risk prediction satisfactory? Stephens JW, Ambler G, Vallance P, Betteridge DJ, Humphries SE, Hurel SJ., Eur J Cardiovasc Prev Rehabil 2004; 11:521528.

2. Cardiovascular risk assessment and screening in diabetes., Zhao, Yanglu, Cardiovascular Endocrinology & Metabolism: March 2017 - Volume 6 - Issue 1 - p 1722

3. Coronary artery disease in type 2 diabetes mellitus: Recent treatment strategies and future perspectives, Ryo Naito and Takatoshi Kasai, World J Cardiol. 2015 Mar 26; 7(3): 119124. , 2015 Mar 26.

4. Comparative performance of diabetes-specific and general population-based cardiovascular risk assessment models in people with diabetes mellitus. Echouffo-Tcheugui JB, Kengne AP. Diabetes Metab 2013; 39:389396.

5. American College of Cardiology/American Heart Association Task Force on Practice Guidelines. 2013 ACC/AHA guideline on the assessment of cardiovascular risk: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. Goff DC Jr, Lloyd-Jones DM, Bennett G, Coady S, D'Agostino RB Sr, Gibbons R, et al. , J Am Coll Cardiol 2014; 63 (Pt B):29352959.

6. Anatomy of coronary disease in diabetic patients: an explanation for poorer outcomes after percutaneous coronary intervention and potential target for intervention. K P Morgan, A Kapur, and K J Beatt, Heart. 2004 Jul; 90(7): 732738.

7. Ostial and midshaft lesions vs. bifurcation lesions in 1111 patients with unprotected left main coronary artery stenosis treated with drug-eluting stents: results of the survey from the Italian Society of Invasive Cardiology ,Tullio Palmerini Diego Sangiorgi Antonio Marzocchi, European Heart Journal Volume 30 Issue 17 September 2009)

8. Intensive Glycemic Control and the Prevention of Cardiovascular Events: Implications of the ACCORD, ADVANCE, and VA Diabetes Trials, Jay S. Skyler, MD, MACP1, Richard Bergenstal, MD2, Robert O. Bonow,Journal of the American College of Cardiology, Volume 53, Issue 3, January 2009

9. Optimal medical therapy with or without PCI for stable coronary disease. Boden WE, O'Rourke RA, COURAGE

Internal Medicine

General Reviews

Trial Research Group. N Engl J Med. 2007; 356: 15031516. doi: 10.1056/NEJMoa070829

10. A randomized trial of therapies for type 2 diabetes and coronary artery disease. The BARI 2D Study Group, Frye RL, N Engl J Med. 2009;360:25032515.

11. 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. Kappetein AP, Head SJ, ; SYNTAX Investigators. Eur J Cardiothorac Surg. 2013;43:10061013. doi: 10.1093/ejcts/ezt017

12. Strategies for multivessel revascularization in patients with diabetes. Farkouh ME, Domanski M, FREEDOM Trial Investigators N Engl J Med. 2012;367:23752384. doi: 10.1056/NEJMoa1211585

13. Strategies for multivessel revascularization in patients with diabetes Farkouh ME, Domanski M, FREEDOM Trial Investigators. N Engl J Med. 2012;367:23752384. doi: 10.1056/NEJMoa1211585.

14. Outcomes with coronary artery bypass graft surgery versus percutaneous coronary intervention for patients with diabetes mellitus: Can newer generation drug-eluting stents bridge the gap? Bangalore S, Circ Cardiovasc Interv. 2014;7:1825

15. Ischemic outcomes after coronary intervention of calcified vessels in acute coronary syndromes. Pooled analysis from the HORIZONS-AMI (Harmonizing Outcomes With Revascularization and Stents in Acute Myocardial Infarction) and ACUITY (Acute Catheterization and Urgent Intervention Triage Strategy) TRIALS. Généreux P, Madhavan MV, Mintz GS , J Am Coll Cardiol. 2014;63:18451854. doi: 10.1016/j.jacc.2014.01.034.

16. Anatomy of coronary disease in diabetic patients: an explanation for poorer outcomes after percutaneous coronary intervention and potential target for intervention. K P Morgan, A Kapur, and K J Beatt, Heart. 2004 Jul; 90(7): 732738.

17. Percutaneous Coronary Interventions in the Diabetic Patient.Where Do We Stand? John A. Bittl, Circulation: Cardiovascular Interventions. 2015;8:e001944

18. Coronary artery disease and diabetes mellitus, Doron Aronson, MD and Elazer R. Edelman, MD, PhD, Cardiol Clin. 2014 Aug; 32(3): 439455. 2014 Jun 10.*

19. Angiographic characteristics of the coronary artery in patients with type 2 diabetes. Tong-guo Wu, MD1 and Lexin Wang, MD PhD. Exp Clin Cardiol. 2002 Winter; 7(4): 199200.