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Case Report

Risk Factors Associated with Repeat Revascularization within 7 Years of First Percutaneous Coronary Intervention in a Diabetic Patient

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Abstract

Background: Despite increased attention to more intensive medical therapy for patients with established coronary artery disease (CAD), the presence of type 2 diabetes mellitus (T2DM) is associated with extended vascular atherosclerotic lesions in sites unrelated to the revascularized segment leading to an increased tendency to postrevascularization target and nontarget vessel ischemic events.

Material and Methods: We report a case of a 66-year-old man with insulin dependent type 2 diabetes patient who has been admitted to the emergency department for an ischemic event: atypical chest pain after physical exertion.

The Aim of the Study: to evaluate the risk factors associated with repeat revascularization within 7 years of first percutaneous coronary intervention (PCI) in a diabetic patient.

Results: On initial evaluation the patient presented with the symptoms of atypical chest pain, confined in the epigastrium, dyspnea. The physical findings of the patient: atrial fibrillation, hypotension, type 2 diabetes with macro- and microangiopathy, chronic kidney disease (CKD), hyperlipidemia, previous revascularization by PCI were revealed. The recent coronary angiography showed multivessel atherosclerotic lesions in sites unrelated to the previously revascularized segments.

Conclusion: The obtained data suggest that the factors associated with repeat revascularization within 7 years of first percutaneous coronary intervention of the presented case are uncontrolled type 2 diabetes mellutis, CKD, dyslipidemia and the progression of atherosclerosis with the involvement of multivessel legions.

Keywords: Coronary Angiography; Percutaneous Coronary Intervention; Repeat Revascularization; Diabetes Mellitus

Abbreviations

PCI: Percutaneous Coronary Intervention; T2DM: Type 2 Diabetes Mellutis; CAD: Coronary Artery Disease; NSTE-ACS: Non-ST Elevation-acute Coronary Syandrome; OMT: Optimal Medical Therapy; DAPT: Dual Antiplatelet Therapy; CKD: Chronic Kidney Disease; MI: Myocardial Infarction; aCx: Circumflex Artery; LAD: Left Anterior Descending Artery; DES: Drug Eluting Stent; IR: Intermediate Artery

Introduction

Diabetes mellitus is associated with extended vascular atherosclerotic lesion leading to increased cardiovascular risk. The progressive nature of CAD in patients with T2DM lead to an increased tendency to postrevascularization target and nontarget vessel ischemic events, especially in those with more advanced T2DM as reflected by insulin requirements [1]. Both surgical and percutaneous revascularization outcomes are impaired in the setting of T2DM, with an increased risk of adverse procedural events

and of long-term lesion development, progression, and restenosis [2,3]. However, as coronary anatomic burden and complexity increase, particularly among those with large ischemic burden or frequent angina, the benefit of revascularization combined with optimal medical therapy (OMT) becomes manifest [4,5].

The individualized consideration of the need for and optimal choice of revascularization strategy is required, becouse the relative benefit and risk of each revascularization strategy vary by the extent and complexity of CAD and the patient's underlying comorbid state [6].

Despite increased attention to more intensive medical therapy for patients with established coronary artery disease (CAD), progressive atherosclerosis in sites unrelated to the revascularized segment commonly contributes to the need for repeat revascularization [7].

As a result of these temporal changes in disease management, repeat revascularization remains common in the first several years after PCI, even after accounting for widespread DES use in contemporary practice [8]. Despite increasing number of complex patients and lesions treated by contemporary PCI, overall repeat revascularization rates remain around 12% at 1 year, and more than one fourth of these repeat procedures are staged interventions related to multivessel CAD. These findings highlight the importance of identifying ischemia-producing stenosis accurately and ascertaining that appropriate secondary prevention therapies are implemented after PCI [9].

Material and Methods

We report a case of a 66-year-old man who had admitted to the emergency department for atypical chest pain after physical exertion, localized in the epigastrium, dyspnea, hypotension.

The Aim of the Study

To evaluate the factors associated with repeat revascularization within 7 years of first percutaneous coronary intervention in a diabetic patient.

Results

Initial evaluation at admission revealed: symptoms of atypical chest pain, confined in the epigastrium, dyspnea. The objective examination and physical findings of the patient detected the medium-severe general condition, determined by moderate angina syndrome, arrhythmic heart sounds. ECG within 10 min detected atrial fibrillation. Monitoring of vital signs showed hypotension 90/65 mmHg, heart rate = 100 bpm and suspicion of cardiogenic shock. Clinical history: stage II hypertension, chronic atrial fibrillation (AF), insulin dependent type 2 diabetes of 15 years, with macro- and microangiopathy, CKD, hyperlipidemia. He experienced non-Q-wave MI of the inferior left ventricular wall and was revascularized by PCI: the approach of severe stenosis on LAD, CX III with the implantation of DES on each lesion (two stents in total), obtaining a good angiographic result.

According to the initial presentation, abdominal disorders (e.g. reflux disease, esophageal spasm, esophagitis, gastric ulcer, cholecystitis, or pancreatitis) also were considered in the differential diagnosis. No differences in blood pressure between the upper and lower limbs or between the arms, irregular pulse, jugular vein distension, heart murmurs, friction rub, and pain reproduced by chest or abdominal palpation, suggestive of alternative diagnoses, were funded.

The electrocardiographic examination of the patient showed the presence of AF and characteristic abnormalities: disturbances of the apical, lateral repolarization processes include ST-segment depression, transient ST-segment elevation, and T-wave invertion > 1mm in 4 leads considering I, avL and V4-V6 (Image 1).

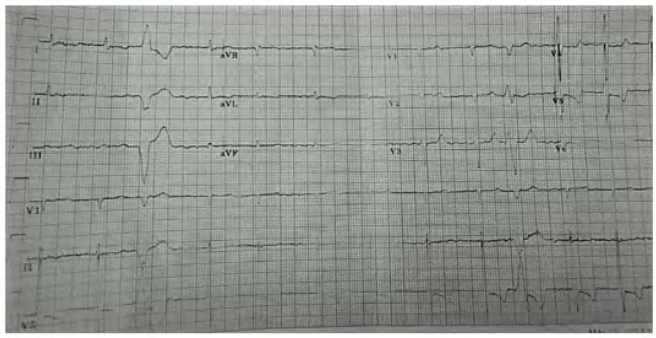

Image 1: Electrocardiographic examination of the patient at the time of admission.

Laboratory tests of cardiac biomarkers on presentation and within 60 minutes cTn results were without changes. The biochemical data detected: increased values of blood glucose - 27.7 mmol/l, creatinine - 369 mmol/l.

On echocardiographic investigation was visualized moderate dilation of right atrium (RA), left atrium (LA), and right ventricle (RV), mild concentric hypertrophy of the interventricular septum (IVS), akinesia of the basal segment of the inferior wall, hypokinesia of the basal and middle segment of the lateral left ventricular (LV) wall and moderate reduced ejection fraction of the LV - 44%.

Chest radiography of the patient detected cardiac enlargement (Image 2).

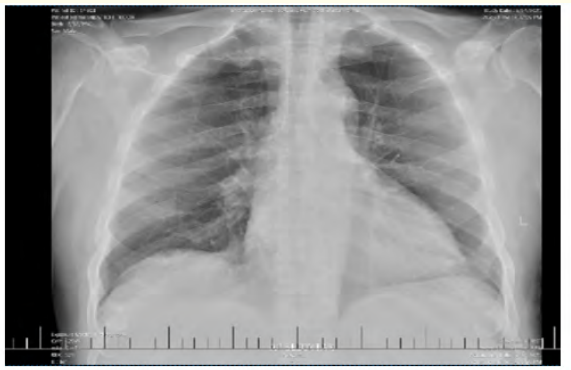

Image 2: Chest x-ray of the patient.

According to the recent Guidelines the patient was transferred to the catheterization laboratory for diagnosis validation and risk assessment and selection for early invasive treatment by revascularization. Optimal medical therapy included: dual antiplatelet therapy with loading dose of aspirin 300 mg and clopidogrel 600 mg on presentation, anticoagulation with 5.000 I.U. of heparin, vasodilators: β-blockers, angiotensin conversion enzyme inhibitors and statins.

The achieved coronary angiography revealed multivessel atherosclerotic lesions: critical 99% subocclusive stenosis on the IR branch, stenosis 75%, moderate-severe on the LAD (DIA I), insignificant on LM, RCA, and aCX, and previously implanted stents on LAD and aCX - with no signs of restenosis. The patient underwent repeat revascularization on IR branch: PCI with implantation of 2 DES in the stenotic segment with the restoration of the arterial lumen (Image 3).

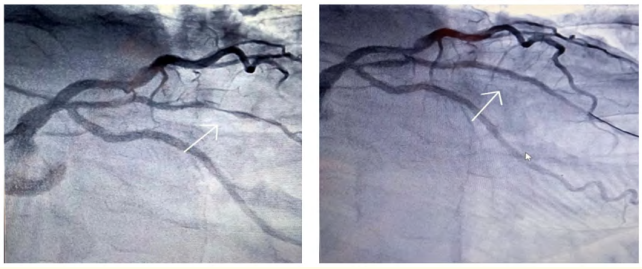

Image 3: Coronary angiography. a) Critical subocclusive stenosis on the IR branch; b) The restoration of the arterial lumen.

He was discharged with the recommendations: double antiplatelet treatment with clopidogrel 75 mg - for 6 months, aspirin 75-100 mg/day, β-blockers, angiotensin conversion enzyme inhibitors and statins for long time.

Discussion

Patients with diabetes more frequently present with non-typical symptoms than patients without diabetes. They more frequently have multifocal CAD, less frequently receive guideline-indicated care, and have worse clinical outcomes [10,11]. Non-typical presentations include isolated epigastric pain, indigestion-like symptoms, and isolated dyspnea or fatigue. Atypical complaints are more often observed in the older patient, in women, and in patients with diabetes, chronic renal disease, or dementia [12]. The exacerbation of symptoms by physical exertion, and their relief at rest, increase the probability of myocardial ischemia. The relief of symptoms after nitrate administration increases the likelihood of NSTE-ACS, but this is not diagnostic as it is also reported in other causes of acute chest pain [13].

Older age, male sex, family history of coronary artery disease (CAD), diabetes, hyperlipidemia, smoking, hypertension, renal dysfunction, previous manifestation of CAD, and peripheral or carotid artery disease increase the likelihood of NSTE-ACS [14,15].

Conditions that may exacerbate or precipitate NSTE-ACS include anemia, infection, inflammation, fever, hypertensive peak, anger, emotional stress, and metabolic or endocrine (particularly thyroid) disorders. Compared with the non-diabetic population, the progress of atherosclerosis in the diabetic group is earlier

and more severe [16-18]. Simultaneously, patients with T2DM are at an increased risk of having a cardiovascular event, and more likely to have diffuse and multivessel vascular lesions [19,20]. Additionally, more complex coronary anatomy usually emerges in the diabetic group, which challenges the revascularization whether coronary artery bypass grafting (CABG) or percutaneous coronary intervention (PCI) [21].

Cardiovascular deaths account for 52% of deaths in T2DM mortality of diabetic patients after myocardial infarction is also significantly higher than that of non-diabetic patients [22-24]. Compared with non-diabetic patients of the same age group, the cardiovascular mortality of patients with no other traditional cardiovascular risk factors increased by 4.4 times [25]. Although the mortality of CAD has been well-controlled with the development of interventional strategies, the prognosis of patients with CAD and T2DM is still very poor [26]. The CAD and T2DM patients are prone to a more rapid progression of atherosclerosis, significantly increasing the need for myocardial revascularization [27]. Besides, patients with T2DM also have a worse prognosis following a coronary revascularization procedure [28].

Percutaneous coronary intervention (PCI) or coronary artery bypass grafting (CABG) is still controversial in patients with coronary artery disease (CAD) and type 2 diabetes mellitus (T2DM). Liang B., *et al*. aimed to evaluate the long-term follow-up events of PCI and CABG in these populations. Relevant randomized controlled trials were retrieved from PubMed, Embase, and the Cochrane databases. The pooled results were represented as risk ratios (RRs) with 95% confidence intervals (CIs) with STATA software. A total of six trials with 1,766 patients who received CABG and 2,262 patients who received PCI were included in our study. Patients in the CABG group were significantly associated with a lower all-cause mortality compared with those in the PCI group (RR = 0.74, 95% CI = 0.56-0.98, P = 0.037). Cardiac mortality, recurrent myocardial infarction, and repeat revascularization were also significantly lower in the CABG group (RR = 0.79, 95% CI = 0.40-1.53, P = 0.479; RR = 0.70, 95% CI = 0.32-1.56, P = 0.387; and RR = 0.36, 95% CI = 0.28-0.46, P < 0.0001; respectively). However, compared with the PCI group, the cerebral vascular accident was higher in the CABG group (RR = 2.18, 95% CI = 1.43-3.33, P < 0.0001). CABG revascularization was associated with significantly lower long-term adverse clinical outcomes, except cerebral vascular accident, compared with PCI in patients with CAD and T2DM [29].

Althouth current percutaneous and surgical revascularisation techniques are associated with excellent procedural and long-term clinical outcomes, a considerable proportion of patients require repeat revascularisation procedures during long-term follow-up due to failure of the initial revascularisation - either PCI or CABG - or progression of disease in previously untreated coronary segments [30]. The predictors of repeat revascularization due to restenosis and/or progression of disease are largely debated. Despite increased attention to more intensive medical therapy for patients with established coronary artery disease (CAD), progressive atherosclerosis in sites unrelated to the revascularized segment commonly contributes to the need for repeat revascularization [31]. Around 20% of patients suffering myocardial revascularization need a repeat revascularization procedure during the first five years of follow-up, with a higher risk after percutaneous coronary interventions (PCI) as compared with coronary artery bypass grafting [32,33].

The requirement for repeat revascularization has a important impact on quality of life and healthcare resources, and exposes patients to risks basically connected to repeat hospitalizations and invasive procedures [34]. The patients needing repeat revascularization are characterized by a high cardiac risk profile, due to comorbidities and anatomical features, interpreting their clinical management a substantial task in daily practice [35]. CAD progression in native coronary segments previously untreated is the primary cause of repeat procedures after myocardial revascularisation. Disease progression is responsible for a relevant proportion of repeat revascularisation procedures after PCI [36]. The aim of the study by Taniwaki., *et al*. was to investigate 4-year outcomes and predictors of repeat revascularization in the RESOLUTE All-Comers trial. Patients were randomly assigned to treatment with the R-ZES (n = 1,140) or the EES (n = 1,152). They assessed pre-specified safety and efficacy outcomes at 4 years including target lesion failure and stent thrombosis. At 4 years, the results showed that rates of target lesion failure (15.2% vs. 14.6%, p = 0.68), cardiac death (5.4% vs. 4.7%, p = 0.44), and target vessel myocardial infarction (5.3% vs. 5.4%, p = 1.00), clinically-indicated target lesion revascularization (TLR) (7.0% vs. 6.5%, p = 0.62), and definite/probable stent thrombosis (2.3% vs. 1.6%, p = 0.23) were similar with the R-ZES and EES. Independent predictors of TLR were age, insulin-treated diabetes, SYNTAX (Synergy between PCI with Taxus and Cardiac Surgery) score, treatment of saphenous

vein grafts, ostial lesions, and in-stent restenosis. Independent predictors of any revascularization were age, diabetes, previous percutaneous coronary intervention, absence of ST-segment elevation myocardial infarction, smaller reference vessel diameter, SYNTAX score, and treatment of left anterior descending, right coronary artery, saphenous vein grafts, ostial lesions, or in-stent restenosis [36].

Although the incidence varies based on the clinical and anatomic characteristics of the population studied. The Prospective Natural History Study of Coronary Atherosclerosis (PROSPECT) studied the relative contribution of events related to the initially treated lesion (culprit lesion) and events related to CAD progression in non-culprit sites [37]. The cumulative rate of major adverse cardiac events - a composite of cardiac death, arrest, MI, and hospitalisation for angina - was 20.4% at three years, with 12.9% of events related to the culprit lesion and 11.6% of events due to CAD progression at non-culprit sites. Overall, 65% of all events occurred within one year after PCI, with a relatively equal distribution between events related to the culprit lesion and those related to CAD progression. The overall repeat revascularisation rate was 17.1% at three years, with an equal contribution of events related to the culprit lesion and those related to CAD progression. The autors concluded that predictors of CAD progression in previously untreated native coronary segments include clinical and angiographic factors that are largely overlapping with predictors of PCI and CABG failure, such as age, diabetes mellitus, complex coronary anatomy, extent of CAD, small vessel CAD, and previous PCI of vein grafts or ostial lesions [38].

In case of CAD progression in previously untreated native coronary segments following revascularisation, treatment recommendations should be based on symptoms and evidence of myocardial ischaemia. In this context, optimal medical therapy plays a pivotal role not only to reduce the risk of CAD progression but also for an initial management of patients with evidence of CAD progression [39,40].

Diabetic patients account for an increasing number of patients undergoing percutaneous coronary intervention. The objective of the study by Sharma A., *et al*. was to evaluate efficacy and safety of short duration DAPT (S-DAPT) and long duration DAPT (L-DAPT) after drug eluting stent (DES) implantation in DM and non-DM patients. There was no significant difference in the rate of all-cause mortality, cardiac mortality, ST, MI, TVR, major bleeding, stroke and NACE with S-DAPT and L-DAPT in DM patients [1.19 (0.72-1.95); 1.25 (0.69, 2.25); 1.52 (0.70, 3.29); 1.33 (0.88, 2.01); 1.39 (0.89, 2.17); 0.92 (0.19, 4.42); 0.98 (0.29, 3.28); and 0.94 (0.57, 1.54) respectively]. Further, there was no significant difference in the rate of all-cause mortality, cardiac mortality, MI, TVR, major bleeding, stroke and NACE with S-DAPT and L-DAPT in non-DM patients 0.93 (0.58, 1.48); 0.75 (0.42, 1.35); 1.52 (0.81, 2.83); 0.99 (0.71, 1.39); 0.72 (0.28, 1.84); 1.01 (0.40, 2.56); and 1.01 (0.77, 1.32) respectively] [41]. The authors concluded that compared to L-DAPT, S-DAPT was associated with significant increase in rate of ST in non-DM patients. Duration of DAPT had no significant impact on rates of all-cause mortality, cardiac mortality, MI, ST and TVR among DM patients [41]. Nonetheless, the selection of antithrombotics and an invasive strategy should not differ from those without diabetes. Compared with clopidogrel, more potent platelet inhibitors have higher absolute risk reductions in patients with diabetes [42,43].

On admission to hospital, it is recommended that all patients with NSTE-ACS have their glycaemic status evaluated, regardless of a history of diabetes, and for it to be monitored frequently in patients with diabetes or hyperglycaemia. Given that, during the acute phase of NSTEMI, there may be hyperglycaemia, there is the potential for a false positive diagnosis of diabetes. Therefore, the diagnosis of diabetes should be confirmed subsequent to the hospital stay. In critically ill patients, there is a risk of hypoglycaemia-related events when using intensive insulin therapy [44]. It is not unreasonable to manage hyperglycaemia in patients with NSTE-ACS by keeping their blood glucose concentration <11.0 mmol/L or <200 mg/dL) while avoiding hypoglycaemia, but intensive insulin therapy should not routinely be offered unless clinically indicated. Intensive lipid modification is indicated for secondary prevention [45].

Conclusion

The obtained data suggests that the factors associated with repeat revascularization within 7 years of first percutaneous coronary intervention of the presented case are uncontrolled type 2 diabetes mellutis, CKD, dyslipidemia and the progression of atherosclerosis with the involvement of multivessel legions. A

multifactorial approach to diabetes mellitus management, with treatment targets, should be considered in patients with diabetes mellitus and cardiovascular disease. The continued evolution of more potent antiplatelet agents and therapeutic regimens has demonstrated promise in reducing risk and preserving safety in a much broader population of patients with T2DM.

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