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SHORT COMMUNICATION

Diabetic patient with three-vessel disease and left main involvement. Surgery yes, but not always

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Abstract Coronary artery disease (CAD) is known to be the main cause of morbidity and mortality in patients with diabetes mellitus. Although they do not often show typical recognized symptoms, diabetic patients suffer from more extensive CAD and hence higher incidence of multi-vessel CAD than in non-diabetic subjects. Literature has given the strength of evidence in favor of surgical revascularization in diabetic patients with multi-vessel disease. We report the case of a 61-year old active smoker and diabetic man with atypical symptoms and positive treadmill test. The coronary angiography revealed a severe three-vessel disease and distal left main involvement (SYNTAX score = 49). As the patient refused to follow heart team indication to undergo coronary bypass grafting, a percutaneous coronary intervention was successfully performed with intra-aortic balloon counterpulsation support and intravascular ultrasound optimization. The mid-term outcome was good.

1. Introduction

The perceivable link between the coronary artery disease (CAD) and diabetes mellitus had been known for many years. The incidence of coronary artery disease (CAD) in diabetics is four times higher compared to the age-adjusted general population.[1] Furthermore, CAD is known to be the main cause of morbidity and mortality in patients with diabetes mellitus (DM).[2] Although they do not often show typical recognized symptoms, diabetic patients suffer from more extensive CAD and hence higher incidence of multi-vessel CAD than in non-diabetic subjects.[3] Multi-vessel coronary artery disease revascularization is commonly performed throughout the world. Among approximately 700,000 patients who undergo multivessel coronary revascularization yearly, 25% have diabetes.[2,4] For the last two decades, there has been intense debate between interventional cardiologists and surgeons regarding the most effective mode of revascularization in patients with diabetes,

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particularly in those with multivessel disease or left main stenosis,[5–8] until the FREEDOM trial gave the strength of evidence in favor of coronary artery bypass grafting (CABG).[9] However, surgical revascularization is not always feasible or accepted by all the patients. Otherwise, although single-center observational data had suggested a reduction in mortality and major complications with the use of an elective intra-aortic balloon pump (IABP) during high-risk PCI,[10,11] the first randomized controlled evaluation of the safety and efficacy of counterpulsation during high-risk PCI did not confirm these findings.[12]

2. Case report

A 61-year old, active smoker (1 peak per day since 40 years) with a history of non-insulin dependent DM for 10 years treated by 2 daily tablets of metformin, sought medical care for easy fatigue and chest discomfort on physical exertion since 10 years exacerbating since 3 months. Clinical examination was normal. Blood tests revealed a preserved renal function preserved (creatinine 0.98 mg/dl and clearance of creatinine 95 ml/mn), a glycosylated hemoglobin of 7.2% and his lipid profile showed a hypercholesterolemia of 6.9 mmol/l. No abnormalities were found in baseline12-lead electrocardiogram. The treadmill test showed ST depression of 4 mm

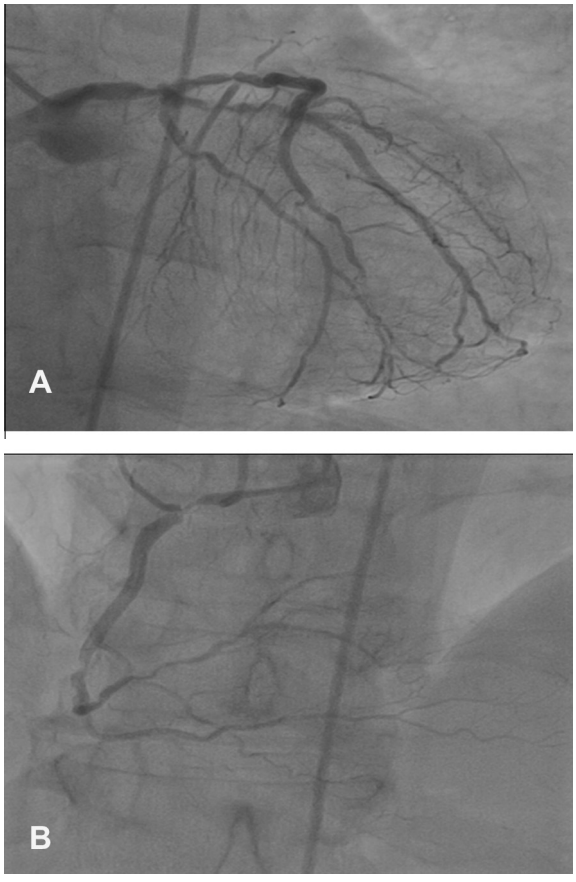

Figure 1 Coronary angiogram: (A) Left coronary angiogram: caudal view showing a distal left main stenosis associated with proximal LAD stenosis and stenosis of the proximal segment of first marginal branch. (B) Right coronary angiogram: cranial view showing a double tight stenosis of the first and the second segments of RCA.

concomitant to the same reported chest discomfort at the second step and the patient was admitted. Trans-thoracic echocardiography found a mildly impaired left ventricular function (ejection fraction 48%) with a moderate global hypokinesia. A coronary angiography was performed: left angiogram revealed calcified distal left main stenosis associated with proximal left anterior descending (LAD) stenosis and a stenosis of the proximal segment of first marginal branch; while right coronary angiogram showed a double tight stenosis of the first and the second segments of RCA (Fig. 1). Risk stratification was performed: operative risk was low with an additive EUROSCORE of 2, while a high SYNTAX score of 49 was found. Although the patient was clearly informed about the heart team decision to opt for surgical revascularization, he refused to undergo CABG; thus the decision to perform PCI was taken. A double femoral 7F access was performed. As considered as high-risk PCI, elective IABP was employed during the procedure. A 6 French Judkins right was engaged in RCA ostium and 2 everolimus-eluting stents (EES) were implanted. Then, a 7 French XB 4 guiding catheter was placed in the left main coronary artery and two guidewires were positioned in LAD and first marginal. After first marginal and proximal LAD angioplasties, a provisional T-stenting of left main was performed with the implantation of one EES. Intravascular ultrasound (IVUS) was employed to assess the apposition of left main stent and a post-dilation was required to optimize it. Final angiographic result was good. Fig. 2 describes the procedure details.

In-hospital stay was uneventful and the patient was discharged after 48 h with the following treatment: aspirin, ticagrelor (dual anti-platelet therapy for 1 year), rosuvastatin, enalapril and atenolol, and addressed to diabetologist for a better control of DM.

At 3 months, the patient was asymptomatic with a negative myocardial scintigraphy. An angiographic control is scheduled after 8 months from the procedure.

3. Discussion

Over the past decades, there has been an extraordinary growth in available modalities for diagnosing and treating CAD. This has resulted in significant decline in the mortality caused by CAD during this period of time.[13,14] Unfortunately, for reasons that are not completely understood, this decline has not been appreciated to the same degree by diabetic patients.[15] The thought that patients with diabetes often have more severe forms of CAD, gives intuitively the impression that they are likely to derive greater clinical benefit from CABG than from PCI. The debate started with the BARI trial which revealed a survival advantage for the subgroup of patients with diabetes treated by CABG rather than angioplasty,[8] and was confirmed in the final 10-year follow-up with respective survival rates of 58% vs 46% ($p = 0.025$).[16] The publications of the 5-year outcomes of the SYNTAX Trial[17] and the ASCERT registry[18] have shown strong evidence that CABG, in comparison with PCI, provides a strong survival benefit as well as a marked reduction in myocardial infarction and repeat revascularization in patients with intermediate and more severe CAD as assessed by SYNTAX scores of >22. The FREEDOM trial randomized 1900 patients with diabetes and multivessel CAD, already receiving aggressive medical therapy, to CABG

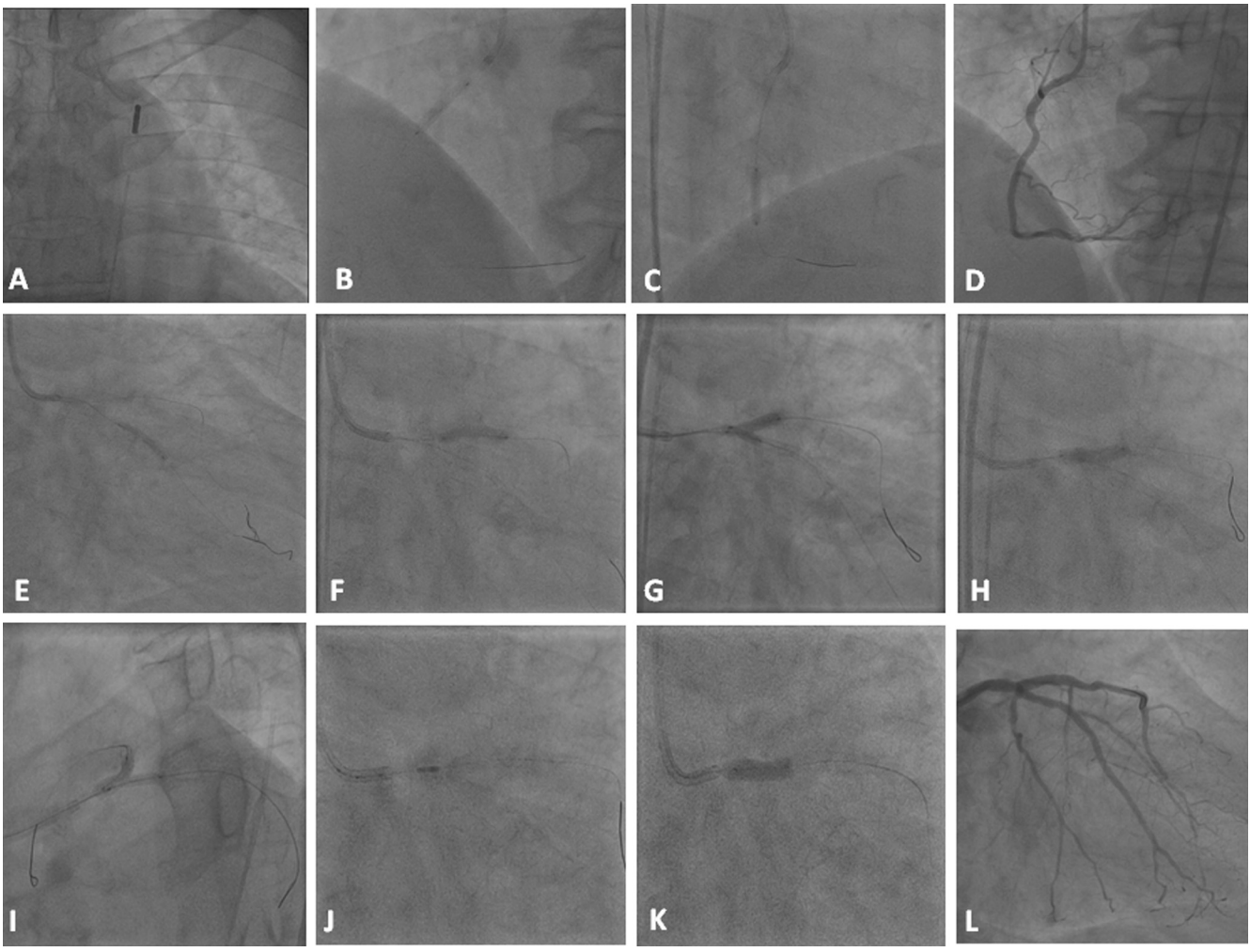

Figure 2 Percutaneous coronary intervention of left main and three-vessel disease. (A) IABP placement; (B) predilation and everolimus DES implantation in proximal RCA (3.0 × 20); (C) predilation and everolimus DES implantation in second segment of RCA (2.75 × 16 mm); (D) good final angiographic result of RCA stenting; (E) predilation and everolimus DES implantation in proximal segment of marginal branch (3.0 × 16); (F) predilation and everolimus DES implantation in proximal LAD (3.0 × 18); (G) predilation with kissing balloon in distal left main lesion; (H) provision stenting of distal left main with everolimus DES implantation (3.5 × 16 mm); (I) kissing balloon; (J,K) optimization of left main result after IVUS. (L) Good angiographic final result in left coronary angiogram.

or PCI with drug-eluting stents.[9] The primary 5-year composite outcome of death from any cause, non-fatal MI or stroke, occurred in 26.6% of the PCI group and 18.7% of the CABG group ($p = 0.005$). The benefit of CABG was driven by superior outcomes in both rates of death from any cause (10.6% vs 14.9%; $p = 0.049$) and myocardial infarction (6.0% vs 13.9%; $p < 0.001$), but at the cost of a higher risk of stroke in the CABG group (5.2% vs 2.4%; $p = 0.03$).[9]

Several other studies have supported the use of CABG rather than PCI in patients with diabetes. In the CARDIa trial,[19] 510 diabetic patients with multi-vessel or complex single-vessel CAD were randomized to PCI or CABG. At 1 year of follow-up, the composite rates of death, myocardial infarction and stroke were 10.5% in the CABG group and 13.0% in the PCI group; all-cause mortality rates were 3.2% and 3.2%, respectively, and the rates of death, MI, stroke or repeat revascularization were 11.3% and 19.3%, respectively.

Evidence from prospective registries also supports the use of CABG rather than PCI in patients with diabetes and multi-vessel CAD.[20] In a large regional database of 7159 consecutive patients with diabetes who underwent coronary revascularization in northern New England 2766 (38.6%) were similar to the patients randomized in the BARI trial. Of this cohort, 736 underwent PCI and 2030 underwent CABG. After adjusting for differences in baseline clinical characteristics, PCI resulted in significantly greater mortality than CABG (HR: 1.49; 95% CI: 1.02–2.17; $p = 0.037$). The mortality risk was greater with PCI in 1251 patients with 3-vessel disease (HR: 2.02; 95% CI: 1.04–3.91; $p = 0.038$) than among 1515 patients with 2-vessel disease (HR: 1.33; 95% CI: 0.84–2.1; $p = 0.21$).

The strength of evidence in favor of CABG should underpin the decision recommendations of the multidisciplinary Heart Team and can also give considerable reassurance to patients and their physicians in recommending this as the optimal revascularization technique in patients with diabetes and multi-vessel CAD who merit intervention and are at low risk for surgery and receptive to this option. However, CABG is not always possible in case of high operative risk, extensive

CAD with a bad distal artery bed, or when the patient refused surgery, as observed in our case; thus, PCI remains despite of its risk an attractive and sometimes the last option.

IABP has been in clinical use for more than 4 decades,[21] largely on the basis of favorable observational data as well as the beneficial effect of counterpulsation on coronary blood flow and myocardial oxygen demand.[22] The widespread use of IABP during high-risk PCI, acute myocardial infarction, and cardiogenic shock[23] had been at odds with the paucity of adequately powered randomized controlled trials in these settings.

The Balloon Pump–Assisted Coronary Intervention Study (BCIS-1)[12] evaluated the effect of elective IABP use on the incidence of major adverse cardiac and cerebrovascular events (MACCE) in patients with severe ischemic cardiomyopathy undergoing PCI. Perera et al.[12] found that in high-risk PCI, prophylactic IABP placement did not reduce 28-day MACCE occurrence. Although patients undergoing IABP placement experienced fewer procedural complications, rates of access complications and minor bleeding were higher. However some issues should be considered. Most important is the definition used for high-risk PCI, which was a combination of impaired left ventricular function (< 30%) and complex CAD. Although this definition is in line with previously conducted studies, no generally accepted guideline-based definition for high-risk PCI currently exists. Indeed, in our case, although the left ejection was relatively preserved, the presence of a tight calcified stenosis of distal left main and three-vessel disease with a SYNTAX score of 49 make us consider the procedure as high-risk PCI. Actually, IABP has class IIb recommendation (level of evidence C) in the current American College of Cardiology Foundation/American Heart Association/Society for Cardiovascular Angiography and Interventions guidelines for PCI and is only recommended in the presence of hemodynamic impairment in the current European Society of Cardiology guidelines on revascularization.[24,25] However, long-term follow-up of BCIS-1 (median 51 months) showed 34% relative reduction in all-cause mortality compared with unsupported PCI.[26]

The use of IVUS in left main intervention is able to evaluate stent underexpansion, incomplete lesion coverage, small stent area, large residual plaque, and stent malapposition which have been found to predict stent thrombosis after drug eluting stent placement.[27,28] In the MAIN-COMPARE registry, Park et al. showed that elective stenting with IVUS guidance, especially in the placement of drug-eluting stent, may reduce the long-term mortality rate for unprotected left main coronary artery stenosis when compared with conventional angiography guidance. Moreover, de la Torre Hernandez et al. showed an association of IVUS guidance during PCI with better outcomes in patients with left main disease undergoing revascularization with DES.[29] Indeed, IVUS-guided procedure was identified as a protective predictor for major adverse events in the overall population (hazard ratio = 0.70) and the distal unprotected left main subgroup (HR = 0.54).[29] In addition, IVUS may also play a role in the selection of the most appropriate stenting technique and the eventual need for a second stent after provisional stenting.[30]

Finally, in addition to the use of hemodynamic support and IVUS guidance optimization, the good outcome of our patient might be due to the relatively preserved ventricular function.

4. Conclusion

According to FREEDOM study, in patients with diabetes and advanced CAD, CABG was superior to PCI reducing rates of death and myocardial infarction. However, because of patients' preference, high operative risk or anatomical reasons, surgery cannot be performed; thus PCI with drug-eluting stents remains a reliable alternative in experienced hands. A hemodynamic support by IABP and IVUS use might be supplementary tools to optimize the outcome.

Conflict of interest statement

None.

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