Bare-Metal Stents for Primary PCI

Challenging the myths with evidence.

BY ANDER REGUEIRO, MD, AND MANEL SABATÉ, MD, PHD

Pharmacological or early mechanical reperfusion should be performed as early as possible for patients with ST-segment elevation myocardial infarction (STEMI). If it can be performed expeditiously, primary percutaneous coronary intervention (PCI) is the preferred reperfusion strategy.[1] Randomized clinical trials comparing primary PCI with in-hospital fibrinolysis have shown that primary PCI is superior to hospital fibrinolysis.[2] During the initial years after the introduction of coronary stents, it was thought that the implantation of a metallic device in a thrombotic environment could increase the risk of adverse outcomes. It was not until the development of newer stent techniques and antiplatelet regimens that the use of stents in STEMI was generalized. The advent of drug-eluting stents (DES) represented a breakthrough in the field, as they appeared to be more efficacious than bare-metal stents (BMS) in many different scenarios,[3,4] including STEMI.[5-7] There is still a common belief, however, that STEMI represents a niche for BMS. In this article, we challenge the issues that appear to support this statement.

MYTH 1: BMS IS LESS THROMBOGENIC IN STEMI THAN DES

Stent thrombosis is an infrequent but serious complication with a high mortality rate. In fact, it can be manifested by fatal and nonfatal STEMI in > 80% of patients, with a mortality rate up to 25% within 30 days.[8,9] Slow coronary flow, stent malapposition and/or underexpansion, stent length, dissection, exposure of the blood to prothrombotic subendothelial tissue, and failure to inhibit platelet adhesion and aggregation are some of the mechanisms of stent thrombosis.[10,11] In most clinical registries, acute coronary syndrome as a clinical condition at the time of the index procedure repeatedly appears as an independent predictor of stent thrombosis.

The timing of stent thrombosis differs between the types of stents. During the first months, it may

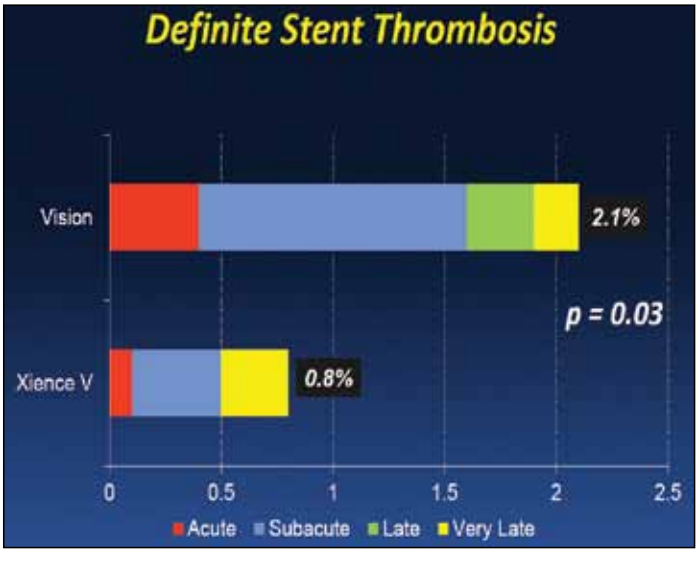

Figure 1. Definite stent thrombosis (according to the American Research Consortium definition) rate between Xience V (everolimus-eluting stent; Abbott Vascular) and Multi-Link Vision (BMS; Abbott Vascular) over 2 years of follow-up.

occur after both BMS and DES implantation; however, beyond 1 year, it is more frequently observed after first-generation DES implantation. Second-generation DES have been evaluated in the setting of STEMI. The EXAMINATION trial compared the performance of a cobalt-chromium everolimus-eluting stent (Xience V, Abbott, Santa Clara, CA) versus a BMS in patients with STEMI, with an all-comers inclusion design. At 1 year, with the use of Xience V, there was a statistically significant reduction in the definite and definite/probable stent thrombosis rates (0.5% vs 1.9% and 0.9% vs 2.5%; both $P = .019$).[6] This benefit was extended out to 2 years (Figure 1).[12] Similarly, Räber et al compared the use of a biolimus-eluting stent with biodegradable polymer (BioMatrix, Biosensors International, Singapore) versus BMS in patients with STEMI. The use of this DES resulted in an almost 50% lower rate of major cardiovascular events at 1 year compared with BMS.[7] A pooled analysis of both trials[13] demonstrated a reduction in both stent thrombosis and target-vessel myocardial infarction by the use of these second-generation DES as compared with BMS. Thus, there is no evidence that BMS are safer than second-generation DES in the context of STEMI.

MYTH 2: DES DOES NOT REDUCE CLINICAL RESTENOSIS IN STEMI

There is a common belief that restenosis of treated lesions supplying infarcted territories may be silent or not clinically relevant and that as a result, the potential clinical benefit of DES to reduce repeat revascularization of the treated arteries may be minimal. It has been demonstrated, however, that restenosis is not always a benign process.[14] To define the clinical relevance of the restenosis in STEMI, it was necessary to design trials that did not include mandatory angiographic follow-up to avoid the potential oculostenotic reflex. In particular, both the EXAMINATION and COMFORTABLE AMI trials had only clinical follow-up.[12,13] In both trials, all adjudicated target lesion revascularizations were ischemia-driven and were significantly reduced by second-generation DES. Again, the use of BMS under this consideration seems not to be justifiable (Figure 2).

MYTH 3: PATIENTS IN POOR CLINICAL CONDITION AFTER STEMI MAY REPRESENT THE HIGHEST RISK CONDITION FOR THROMBOSIS

Patients in cardiogenic shock may be a niche for BMS due to the lack of evidence of DES superiority in this context. In addition, patients undergoing mild hypothermia therapy in the context of sudden death secondary to ventricular fibrillation and STEMI may represent another cohort at high risk of stent thrombosis.[15] Several factors may favor stent thrombosis in this scenario: first, impaired absorption of antiplatelet agents in cardiogenic shock or under hypothermia [16]; second, enhanced thrombogenicity and impaired antithrombotic effect under these conditions [17]; third, the potential for thrombosis in the rewarming phase; and finally, the difficulty of sizing stents for patients in shock, which may lead to underexpansion, malapposition, and further thrombosis. Given the poor neurologic and cardiologic outcomes of this type of patient, BMS may be the preferred option, specifically in countries where DES are more expensive than BMS.

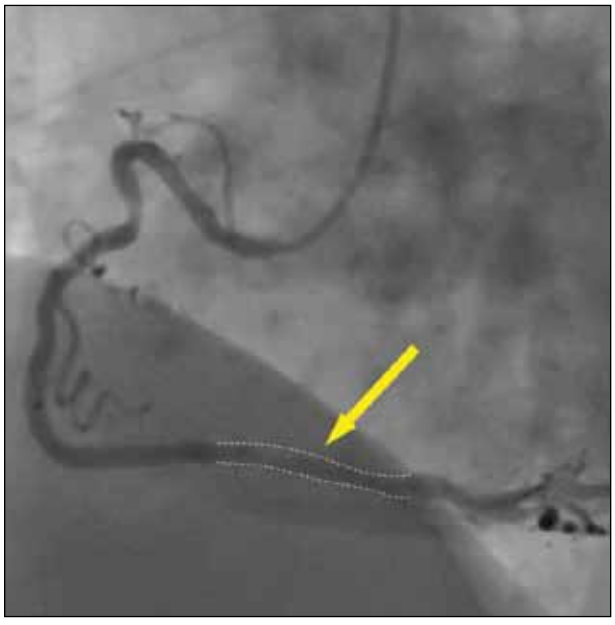

Figure 2. Diffuse in-stent restenosis (yellow arrow) of a BMS (white dots) in the distal right coronary artery implanted 6 months earlier for the treatment of an inferior STEMI.

MYTH 4: IT IS IMPOSSIBLE TO ENSURE 1-YEAR COMPLIANCE OF DUAL-ANTIPLATELET AGENTS IN A PATIENT WITH STEMI

Indeed, this is true. Current guidelines propose dual-antiplatelet therapy for 1 year, however, regardless of the type of stent.[1,18] Thus, in the general population, this concern applies for either stent type. Measures to ensure good patient compliance after discharge should be implemented at the general practitioner or outpatient clinic. Current data on the use of second-generation DES is reassuring regarding shortening the duration of dual-antiplatelet therapy even in patients

with acute coronary syndromes.[19] However, it remains to be demonstrated whether this is applicable to the STEMI population that is noncompliant with a dual-antiplatelet regimen.

MYTH 5: STEMI IN ELDERLY PATIENTS REPRESENTS A POPULATION NOT SUITABLE FOR DES

It is a common belief that elderly patients represent a population not suitable for DES. This cohort of patients may present several comorbidities that preclude good compliance with any type of treatment. In addition, they are often excluded from trials. Thus, it is difficult to set a clear indication for DES, and individualized decisions should be undertaken.

Recently, the results of the XIMA trial have been presented.[20] XIMA is an international, multicenter, prospective, randomized trial to examine the safety and efficacy outcomes among octogenarians with either a BMS or cobalt-chromium everolimus-eluting stent (Xience V) implantation for complex coronary disease in the context of stable angina or an acute coronary syndrome. The trial enrolled 800 patients aged 80 years or older. Both target vessel revascularization and myocardial infarction were reduced in the Xience V arm as compared to the BMS arm. There was no difference in mortality between the two groups and no difference in the rates of major bleeding or stroke at 1 year. Whether these data are applicable to STEMI patients older than 80 years remains to be demonstrated.

MYTH 6: STEMI AND ATRIAL FIBRILLATION IS A BAD COMBINATION FOR DES

Atrial fibrillation in the setting of STEMI is estimated to occur in up to 20% of patients, and it is associated with a significant increase in mortality.[21] Bleeding in patients on triple therapy (clopidogrel plus aspirin) is very prevalent. Data from registries show that 29% of patients discharged with atrial fibrillation and myocardial infarction received oral anticoagulant treatment. Chronic oral anticoagulation therapy is associated with a high rate of major adverse cardiac events after PCI.[22] Recently, the WOEST (What is the Optimal Antiplatelet and Anticoagulant Therapy in Patients With Oral Anticoagulation and Coronary Stenting) trial tackled this issue.[23] WOEST was an open-label, multicenter, randomized, controlled trial in 15 centers in Belgium and the Netherlands. From November 2008 to November 2011, adults receiving oral anticoagulants and undergoing PCI were assigned clopidogrel in addition to warfarin (double therapy) or clopidogrel and aspirin in addition to warfarin. The primary outcome was any bleeding episode within 1 year of PCI, assessed by intention to treat. A total of 573 patients were randomized. Twenty-eight percent of patients presented with acute coronary syndromes, and 65% received a DES. Bleeding episodes were significantly reduced in the group of patients receiving double therapy, with no increase in thrombotic or cerebrovascular complications. Although these results were reassuring, we should highlight the fact that this trial was not specifically addressed to STEMI patients and was not powered to show differences in stent thrombosis rates.

The ongoing GLOBAL LEADERS all-comers trial, involving 16,000 patients, will address the effectiveness of 1 month of ticagrelor plus aspirin followed by 23 months of ticagrelor versus a current-day intensive dual-antiplatelet therapy in patients undergoing DES implantation. Although the trial will exclude patients on oral anticoagulants, the information obtained by this study (together with that of the WOEST trial) could shed light on the new antithrombotic regimen in the setting of second-generation DES implantation.

CONCLUSIONS

If we remove any economic consideration from the equation (ie, price of the stent), it is difficult to find a scientific reason to support the use of BMS in STEMI. Current second-generation DES appear to be not only more efficacious but also safer than BMS, even in STEMI. The recommended duration of dual-antiplatelet therapy according to current guidelines in STEMI is independent from the type of stent. In patients requiring oral anticoagulant therapy, the removal of aspirin may minimize the risk of bleeding without any hazard of thrombosis. Elderly patients with STEMI may even benefit from DES, if data from XIMA can be corroborated in STEMI patients. Elderly patients, together with patients in cardiogenic shock or under therapeutic hypothermia, still represent a gap in evidence for the use of DES in the setting of STEMI. In those contexts, we still may give the chance for a BMS implantation. ■

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