

Multivessel Stenting in the Current DES Era

A case report and discussion.

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Until the recent concerns about late and very late thrombosis with drug-eluting stents (DESs), the advent of these devices was greeted with great enthusiasm as one of the final tools needed for unparalleled long-term success with percutaneous revascularization. The RAVEL trial,¹ utilizing a sirolimus-eluting stent, revealed no in-stent restenosis in relatively simple lesions. The subsequent SIRIUS trials with sirolimus-eluting stents and the numerous TAXUS trials with the paclitaxel-eluting stents revealed marked and consistent reductions in endpoints in increasingly complex lesions.²⁻⁸ The use of these devices in allcomers as studied in the RESEARCH and T-SEARCH registries by Dr. Patrick W. Serruys, and the personal experiences of interventionists with DESs, have led to an expansion of their use to ever more complex cases.⁹

Andreas Gruentzig, MD, performed the first successful angioplasty in 1977,¹⁰ and it was not long before comparisons were made between surgical and percutaneous approaches to revascularization. However, as soon as the results became available, they soon appeared obsolete, with changing medical therapy, newer interventional devices, and newer surgical techniques. The initial angioplasty versus surgery trials in multivessel disease, including ERACI I, GABI, EAST, CABRI, and BARI, did not show any mortality differences, but did reveal an increased rate of the need for revascularization and recurrent angina in the percutaneous transluminal coronary angioplasty arms.¹¹⁻¹⁵ However, the subgroup of patients with diabetes appeared to benefit from a surgical approach.¹⁵

With the development of bare-metal stents and their validation in 1994 (STRESS and BENESTENT I),^{16,17} the next set

of randomized trials comparing bare-metal stents to coronary artery bypass grafts were underway, including ERACI II and ARTS I for multivessel coronary artery disease.¹⁸⁻²¹ These studies did not reveal any mortality benefit, and there was a narrowing of clinical outcomes to 14% in ARTS I compared to the pre-stent CABRI.

Not long after these studies were available came news of DESs with the promise of abolishing the Achilles' heel of angioplasty: restenosis. The debate continues, with surgeons noting that previous trials looked at highly selected patients at relatively low risk and preserved left ventricular function, who were not representative of the types of patients who usually undergo surgery, and with interventionists arguing that with DESs, the whole equation has changed.

DRUG-ELUTING STENTS

The results of ARTS II presented by Dr. Serruys, comparing the results of multivessel stenting with DESs to historical outcomes with bare-metal stents and coronary artery bypass grafting (CABG) from ARTS I revealed favorable results, with an 89.5% event-free outcome at 1 year. ERACI III, a similar but smaller study, revealed an increased need for revascularization compared to CABG in ERACI II for the DES group, but a lower mortality rate.^{22,23} There is also an abundant amount of registry outcome data from RESEARCH and T-SEARCH in patients with multivessel coronary artery disease, with encouraging data.

The SYNTAX trial,²⁴ comparing stenting with DESs to CABG in multivessel coronary artery disease, and the FREEDOM trial, studying diabetic patients, should help clarify the role of percutaneous coronary intervention (PCI) with



Figure 1. Thrombotic severe tandem lesions in the right coronary artery (RCA) with TIMI 2 flow.

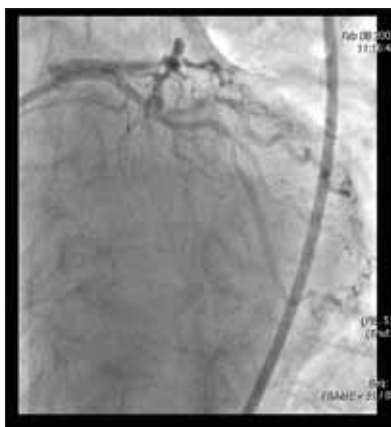


Figure 2. Distal left circumflex artery stenosis.



Figure 3. Sequential diffuse proximal and mid LAD stenosis.



Figure 4. The RCA after thrombectomy and stenting with a 3.5- X 28-mm Taxus stent.



Figure 5. The left circumflex artery after stenting with a 3- X 20-mm Taxus stent.

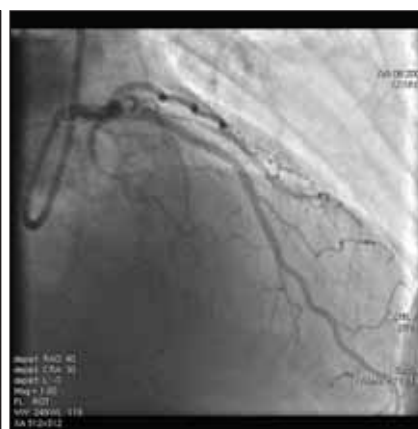


Figure 6. The LAD artery after stenting with 2.5- X 24-mm, 3- X 32-mm, and 3.5- X 12-mm Taxus stents.

DES in these patients. In the interim, however, how do we decide on whom to perform multivessel PCI with DES, a procedure that is currently off-label? I present two examples of multivessel PCI.

CASE REPORTS

Case 1

A 54-year-old man was admitted at an outlying facility with an acute ST elevation inferior wall myocardial infarction with right ventricular involvement. The patient received thrombolytic therapy and intravenous heparin. After 60 minutes, the patient continued to have chest pain and hypotension and was air transferred to our facility for rescue angioplasty.

Coronary angiography revealed thrombotic tandem severe lesions in the right coronary artery with TIMI 2 flow (Figure 1). In addition, there were also severe lesions in the

left circumflex and left anterior descending artery (LAD) (Figures 2 and 3). Using a 7-F, JR4 guide catheter (Abbott Vascular, Santa Clara, CA) and a BMW wire (Abbott Vascular), the right coronary artery was negotiated. Intravenous glycoprotein IIb/IIIa (abciximab) was administered in addition to heparin. We performed mechanical aspiration thrombectomy using a Fetch catheter (Possis Medical, Inc., Minneapolis, MN). Primary stenting using a 3.5- X 28-mm Taxus stent (Boston Scientific Corporation, Natick, MA) was performed with resultant TIMI 3 flow (Figure 4). The patient was stabilized with reperfusion and inotropic support. He was brought back to the catheterization laboratory for LAD artery and circumflex artery intervention the next day. The circumflex artery was treated using a 3- X 20-mm Taxus stent. The LAD artery was treated using 2.5- X 24-mm, 3- X 32-mm, and 3.5- X 12-mm Taxus stents with intravascular ultrasound (IVUS) guidance



Figure 7. Severe stenoses of the mid LAD artery and left circumflex artery.

(Atlantis SR Pro, Boston Scientific Corporation) (Figures 5 and 6). He was discharged 2 days later without any complications, on aspirin indefinitely and clopidogrel for 1 year, along with other cardiac medications.

Case 2

A 52-year-old woman with a long history of tobacco abuse and symptomatic chronic obstructive pulmonary disease, but no previous history of coronary artery disease or diabetes mellitus, was admitted with unstable angina and a small non-ST-elevation myocardial infarction. Coronary angiography revealed an ulcerated 90% stenosis of the mid LAD artery, 70% stenosis of the proximal left circumflex artery, and 90% stenosis of a large obtuse marginal (OM) (Figure 7). The right coronary artery had diffuse and sequential 70% to 90% lesions in the mid and distal RCA (Figure 8). Her left ventricular ejection fraction was preserved at 60%. The option of CABG versus multivessel PCI was presented to the patient, who rejected any consideration of surgical revascularization.

A decision was made to intervene on the left coronary circulation because the LAD artery was believed to be the culprit vessel. A 6-F, geometric left 3.5 guide catheter (Abbott Vascular) was used, and the patient was anticoagulated with unfractionated heparin, abciximab, and dual antiplatelet therapy. The LAD artery lesion was crossed with a 190-cm BMW wire, and IVUS imaging was performed utilizing a 20-MHz Eagle Eye catheter (Volcano Therapeutics, Inc., Laguna Hills, CA) with automated pullback and virtual histology, which



Figure 8. Severe tandem lesions in the RCA.

revealed severe concentric stenosis with multiple areas of necrotic tissue. The LAD artery was predilated with a 2.5- X 15-mm Voyager balloon (Abbott Vascular) and then stented with a 3.5- X 23-mm Cypher stent (Cordis Corporation, a Johnson & Johnson company, Miami, FL). The stent was post-dilated with a 4- X 13-mm Powersail (Abbott Vascular) at high pressures. Repeat IVUS revealed excellent stent apposition with uniform stent expansion. Subsequently, the left circumflex and OM lesions were crossed with a BMW wire, and IVUS guided stenting of the left circumflex/OM was performed. The lesions were predilated with a 2.5- X 15-mm Voyager and stented with 3.5- X 33-mm and 3.5- X 13-mm Cypher stents and postdilated with a 3.5- X 15-mm semicompliant Powersail balloon (Figure 9).

A decision was made to stage the intervention to limit the patient's exposure to contrast and radiation. However, given the severity of the right coronary artery stenosis, she was scheduled for her intervention as an inpatient, as opposed to her returning as an outpatient at a later date.

A 6-F JR4 guide was used to engage the right coronary artery, and the lesions were crossed with a 190-cm BMW wire. A second 190-cm BMW wire was placed in the right coronary artery to act as a buddy wire, and the lesions were predilated with a 2.5- X 20-mm Voyager balloon, stented with 3- X 33-mm, 3.5- X 33-mm, and 3.5- X 18-mm Cypher stents, and postdilated with a 3.5- X 18-mm Powersail balloon. Bivalrudin was used for anticoagulation (Figure 10).

The patient underwent repeat coronary angiography for atypical chest pain 6 months later, which revealed widely patent stents in the right coronary artery, LAD artery, and



Figure 9. The left circumflex and LAD arteries after IVUS guided stenting (3.5- X 33-mm and 3.5- X 13-mm Cypher stents postdilated with a 3.5- X 15-mm Powersail in the left circumflex artery; 3.5- X 23-mm Cypher stent postdilated with a 4- X 13-mm Powersail in the LAD).

left circumflex artery. Nuclear stress testing at 1 year revealed no areas of ischemia and infarction and normal left ventricular function. Clinical follow-up in January 2007, 15 months after the index revascularization, revealed that the patient was asymptomatic. She had to discontinue dual antiplatelet therapy due to recurrent gastrointestinal bleeds after only 7 months but was able to continue on aspirin.

This case highlights factors that may steer one toward PCI versus CABG:

- The patient's preference was important in this case;
- The patient was at increased risk for CABG due to significant chronic obstructive pulmonary disease;
- There was no concern about medical compliance;
- Angiographically, the lesions were amenable to PCIs; and
- The patient was not diabetic.

Technical aspects worth considering include:

- Decision to stage the procedure to limit contrast and radiation exposure;
- IVUS imaging to optimize and plan stent placement;
- Adequate pretreatment of lesions;
- Adequate poststent dilatation with non- or semicompliant balloons, especially in longer lesions and fibrocalcific lesions; and
- Consideration of the use of glycoprotein IIb/IIIa inhibitors in patients with acute coronary syndrome, abnormal troponins, and ulcerated lesions who have not been pretreated with clopidogrel bisulfate.



Figure 10. The RCA after stenting with 3- X 33-mm, 3.5- X 33-mm, and 3.5- X 18-mm Cypher stents, and postdilatation with a 3.5- X 18-mm Powersail balloon.

ANGIOGRAPHIC CONSIDERATIONS

The decision as to whether a surgical or interventional approach is pursued often depends on the angiographic findings. The presence of a chronic total occlusion (CTO) in a major vessel with unfavorable characteristics for percutaneous recanalization may result in a referral for CABG. Success rates for CTO recanalization in trials are approximately 60%. With two chronic total occlusions, CABG is an even more attractive option.

The presence of long lesions with multiple true bifurcation lesions in the same vessel, especially in diabetics, may sway one to a surgical approach in light of concerns about increased stent thrombosis (3%) in such patients. The presence of concomitant unprotected left main artery disease might result in a surgical referral.

PHARMACOLOGIC CONSIDERATIONS

An important consideration that needs to be incorporated into the decision-making process is whether the patient can take aspirin (indefinitely) and clopidogrel bisulfate in an uninterrupted manner for at least 1 year and possibly longer. The success of DESs is intertwined with clopidogrel bisulfate, especially in light of reports of stent thrombosis associated with the premature withdrawal of clopidogrel bisulfate.

Although the instructions for use for the Cypher stent and for the Taxus stent recommend dual antiplatelet treatment for 3 months and 6 months after intervention, respectively; current practice norms would advocate at least 1 year and possibly longer, especially in higher-risk subsets, such as

multivessel coronary artery disease, left main artery, and bifurcation stenting.

Therefore, patients with a history of medical noncompliance, the need for surgery in the upcoming year (which would necessitate the withdrawal of clopidogrel bisulfate), or concerns about bleeding, might be less desirable patients for multivessel PCI with DESs.

CLINICAL CONSIDERATIONS

As our patients become older and present with increasing comorbid issues, including, but not limited to, advanced pulmonary disease, severe left ventricular dysfunction, previous CABG with failed grafts, severe cerebrovascular disease, and cardiogenic shock with end-organ failure, patients are increasingly being referred back to interventionists by surgeons due to unfavorable surgical risk profiles.

The availability of percutaneous hemodynamic support, such as the TandemHeart (Cardiac Assist, Inc., Pittsburgh, PA) and Impella device (Impella Cardiosystems AG, Aachen, Germany) has allowed this paradigm shift, in which patients considered too high risk are frequently referred for PCI instead of CABG.

Patients with renal insufficiency can develop renal failure requiring hemodialysis with both PCI and CABG. Attempts to minimize this risk should include adequate hydration with sodium bicarbonate solution or normal saline, use of as little dye as possible, use of nonionic iso-osmolar dye, pretreatment with acetylcysteine, and staging of the procedure if appropriate. Newer approaches to prevent contrast-induced nephropathy, such as intrarenal infusion of fenoldopam using the Benephit catheter (FlowMedica, Inc., Fremont, CA) are also under investigation, with encouraging results in pilot studies.

OTHER CONSIDERATIONS

Patient preferences play a significant role. Therefore, even patients with unfavorable angiographic characteristics may undergo multivessel PCIs with the understanding that complete revascularization may not be possible.

STRATEGIES

Most multivessel PCIs do not require any specific preparations. However, staging of the procedures should be considered if one or more of the lesions is challenging, as this will help to limit the patient's radiation and contrast exposure.

When one or more of the lesions is a CTO in which revascularization is desirable, a general rule would be to tackle the CTO first, especially if the patient is also a surgical candidate. This allows for default surgery if the CTO cannot be crossed.

Screening for calcium is important to allow adequate pre-

treatment of the lesions, which may include the use of rotational atherectomy before stent implantation. IVUS guidance can be very helpful in longer lesions, proximal LAD artery lesions, and calcified lesions to ensure excellent stent sizing and deployment.

CONCLUSIONS

Currently, 60% of all coronary interventional procedures with DES in the US are off-label. The short- and intermediate-term outcomes with DES show robust decreases in major adverse cardiac events, driven primarily by a decrease in the need for repeat revascularization. However, the longer-term data, as published recently in the *New England Journal of Medicine*, raise some concerns about very late thrombosis between 1 and 4 years (however, without increased mortality).²⁵⁻²⁹ Of note, these patients tended to receive dual antiplatelet therapy for 2 to 6 months only.

Additional DESs on the horizon include the Endeavor stent (Medtronic Inc., Minneapolis, MN), coated with zotarolimus, and the Xience (Abbott Vascular) and Promus (Boston Scientific) stents, coated with everolimus. The Conor stent (Johnson & Johnson, Miami, FL) provides the ability to deliver different drugs both into the wall of the vessel and into the lumen, which may theoretically allow simultaneous antirestenotic therapy and local antiplatelet therapy or prohealing treatments. With improvements in polymers, including bioabsorbable polymers, there is hope for improved healing, which should reduce the need for prolonged dual antiplatelet therapy.

Currently, ongoing randomized controlled trials, such as the SYNTAX and FREEDOM trials, are evaluating multivessel DES versus bypass surgery in different subsets of patients and will provide useful insight into which group benefits greater from individual therapy.

In the interim, given the lack of conclusive long-term data in patients with multivessel coronary artery disease who receive DESs, treatment decisions need to be individualized.

Patient preference, patient compliance with dual antiplatelet therapy, surgical risk, angiographic characteristics, left ventricular function, and comorbid issues, including diabetes mellitus, need to be weighed. ■

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