A case report of the new Polyzene™-F COBRA PzF™ Nancoated Coronary Stent System (NCS): Addressing an unmet clinical need

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1. Introduction

Even with the use of new-generation drug-eluting stents (DES), stent thrombosis and major adverse cardiac and cerebrovascular events (MACCE; composite of death, myocardial infarction or stroke) continue to be clinical risks associated with coronary stent placement. Mitigation of these risks is accomplished with consideration of the patient’s comorbidities and stent selection. Typically, stent choice requires pharmacologic antiplatelet medication for a minimum of 1 month of dual antiplatelet therapy (DAPT; combination of ASA and a P2Y12 inhibitor) post bare metal stent (BMS) placement or for a minimum of 6–12 months DAPT after placement of a drug-eluting stent (DES) per ACCF/AHA/SCAI 2011 PCI and ESC/EACTS 2014 Guidelines on elective percutaneous coronary intervention (PCI) [1,2,3].

Patients treated for atrial fibrillation (AF) are at additional risk when undergoing PCI. Combining chronic oral anticoagulation (OAC) therapy with DAPT, resulting in triple antithrombotic therapy, has been and continues to be intensely scrutinized. Prevention of thromboembolic (stroke) and atherothrombotic (stent thrombosis) events is balanced against the increase risk of severe bleeding in all, but in particular, the triple therapy patients [4]. Careful deliberation includes reducing the duration of or eliminating one or more antithrombotic medications as well as consideration of alternative stent designs for patients at higher risk of bleeding events.

A middle ground in stent design, available through use of Polyzene™-F nano-coating, is designed to impart thrombo-resistance and reduce in-situ inflammation. This coating on the COBRA PzF Coronary Stent System offers a compromise position by shortening DAPT duration to one month with the potential of reducing restenosis incidence. Patients who are not DES candidates or who are at higher risk for bleeding events have been targeted initially for treatment with the COBRA PzF Coronary Stent System and this report provides a description of one of the first uses of the device system with its special properties.

2. Case report

A 72-year-old female with a history of significant comorbidities, including atrial fibrillation, angina (CCS III), arterial hypertension, heart failure, hyperlipidemia, diabetes mellitus type 2 and history of ischemic stroke, was diagnosed with a 75% stenotic mid-LAD lesion; see Fig. 1. Additional risk assessments included a CHA2DS2-VASc score of 7, which is associated with a 9.6% per year risk of stroke without warfarin treatment [5,6], and a HAS-BLED score of 4, which is associated with a 4.9%–19.6% one year bleeding risk while on oral anticoagulants [7]. This particular subject’s specific, but not atypical, profile places her at significant bleeding risk so appropriate stent selection was critical. In April 2014, she received a cobalt chromium alloy COBRA PzF Stent with Polyzene™-F nano-coating (CeloNova BioSciences, Inc., San Antonio, Texas). The COBRA PzF Stent (CE marked) is indicated for improving coronary luminal diameter in patients with symptomatic ischemic heart disease due to coronary artery lesions and is intended for use in patients eligible for percutaneous transluminal coronary angioplasty (PTCA, PCI) with reference vessel diameter of 2.5–4.0 mm.
ECGs, in-hospital and at 30, 180 and 270 days post-procedure. The

2.2. Follow-up

No medication compliance concerns were noted. Aspirin was stopped after 4 weeks, in accordance with the consensus document regimens may also have a reduction of hemorrhagic infarcts. A s p i r i n INR controls and require as few tablets as possible. This anticoagulation to rivaroxaban after 4 weeks was made on the patients’ desire to avoid daily. The modified, targeting an INR of 2.0 — 2.5, during the same 4 week period, after which rivaroxaban (20 mg), a direct factor Xa inhibitor, was prescribed daily. The modification in anticoagulation regimen from phenprocoumon to rivaroxaban after 4 weeks was made on the patients' desire to avoid INR controls and require as few tablets as possible. This anticoagulation regimen may also have a reduction of hemorrhagic infarcts. Aspirin was stopped after 4 weeks, in accordance with the consensus document. No medication compliance concerns were noted.

2.2. Follow-up

To date, the patient has not experienced any adverse or serious adverse events. Assessments have been made, including clinic visits and ECGs, in-hospital and at 30, 180 and 270 days post-procedure. The patient has reported a decrease in symptoms and increased physical activity has been observed.

3. Discussion

Many clinicians agree that use of a BMS, where possible, limits triple therapy duration by restricting DAPT to one month. Conversely, current thinking suggests DES selection increases the duration of triple therapy to 3—6 months. However, with the use of the COBRA PzF™ Coronary Stent System, DAPT can be limited to one month but the restenosis incidence falls in line with a DES.

Stent selection is based on thorough risk assessment of factors each individual presents, coupled with attributes and characteristics of the intended stent. Each device has an inherent risk/benefit profile when factoring the best course of action for a particular patient’s comorbidities and anatomy. The decision between implantation of a BMS, DES or, a bioabsorbable stent, whose scaffold is absorbed after 1—2 years, has included a concomitant cocktail of antithrombotic pharmacologic agents and their respective duration of administration, in the determination.

With its ultra-thin F nano-coating ($0.05 \mu m$) of Polyzene(TM) on a cobalt chromium alloy, thin strut stent platform, the COBRA PzF Coronary Stent, designed to provide flexibility, stability and support, offered the patient described in this report a successful clinical balance of stent selection and DAPT duration. While the stent coating is approximately 100 times thinner than typical DES coverage, the Polyzene(TM)-F material has demonstrated decreased platelet adherence and aggregation, while decreasing inflammation and facilitating re-endothelialization. In the longer term, the surface material has been reported to decrease neointimal proliferation, late loss and restenosis rate. Researchers have speculated that albumin’s preferential binding to Polyzene(TM)-F provides favorable conditions for stent strut endothelialization. This observation is thought to be responsible, in part, for the positive clinical results seen with Polyzene(TM)-F material on the Catania(TM) stent in the ATLANTA and ATLANTA 2 studies that demonstrated a 3.6% clinically-driven target lesion restenosis rate, with no deaths, strokes or myocardial infarctions (MIs), in 55 patients and 6.5% all target lesion restenosis rate in 300 patients with 0% late stent thrombosis (>30 days) recorded at 12 months in both studies. With respect to atherothrombotic events, it has been shown that an increased risk of late stent thrombosis is associated with a morphometrically determined ratio, i.e., uncovered to total struts per section. An optical coherence tomographic comparison, within the same patients, of stent endothelialization showed greater coverage on the Polyzene(TM)-F coated struts at 7—10 days and at 28—32 days post implantation when compared to DES and BMS struts and a lower uncovered to total strut ratio for the Polyzene(TM)-F coated struts at all time points, except when it was not different from the DES struts at the later time point. Reduction of antithrombotic medications associated with the use of the COBRA PzF™ Coronary Stent System, both in the decrease of duration and elimination of multiple pharmacologic agents can be further appreciated when reflecting on a large scale, nationwide, retrospective registry on 40,812 patients diagnosed with a first-time MI. Bleeding incidence, defined as a hospital admission with a diagnosis of non-fatal bleeding (primary or secondary) or a diagnosis of bleeding as the cause of death (futility), was 2.6% for the ASA group, 4.6% for clopidogrel, 4.3% for vitamin K antagonist, 3.7% for ASA plus clopidogrel, 5.1% for ASA plus vitamin K antagonist, 12.3% for clopidogrel plus vitamin K antagonist, and 12.0% for triple therapy. When the data were normalized, using aspirin as a reference value of 1, adjusted hazard ratios for bleeding risk were 1.33 (95% confidence interval 1.11—1.59) for clopidogrel, 1.23 (0.94—1.61) for vitamin K antagonist, 1.47 (1.28—1.69) for ASA plus clopidogrel, 1.84 (1.51—2.23) for aspirin plus vitamin K antagonist, 3.52 (2.42—5.11) for clopidogrel plus vitamin K antagonist, and 4.05 (3.08—5.33) for triple therapy. Selection of the antithrombotic agents, alone and in combination, is clearly an important consideration in reducing bleeding risk.
In a more current, prospective, double-blind, placebo-controlled, phase III trial, 15,526 patients within 7 days of acute coronary syndrome were randomly assigned (1:1:1) to receive twice daily doses of either 2.5 mg or 5 mg of rivaroxaban or placebo for a mean of 13 months [21]. Both doses of rivaroxaban reduced the primary efficacy composite endpoint, death from cardiovascular causes, MI or stroke, as compared with placebo. However, for subjects with atrial fibrillation, only the lower dose of rivaroxaban resulted in an increased survival benefit. In part, this finding was explained by the authors due to the increase in fatal bleeding associated with the higher dose of rivaroxaban.

As is typical in patients with significant coronary artery disease and atrial fibrillation, the patient who is the subject of this manuscript was required to undergo triple therapy, based on her CHA2DS2-VASc score of 7 and a HAS-BLED score of 4, she was at high risk for embolic and bleeding events. However the duration of her triple therapy medication regimen was limited to one month, which lowered the bleeding risk for this patient. DAPT duration and oral anticoagulation have to be considered carefully and be as short as possible. The dosages of 2.5 mg or 5 mg b.i.d of rivaroxaban are based on the ATLAS ACS 2-TIMI 51 trial. This trial studies patients with ACS and how rivaroxaban reduces cardiovascular death, MI, or stroke in patients following ACS, and cannot be extrapolated to patients with atrial fibrillation and stable CAD. The patient in this manuscript had no ACS, normal renal function and takes NOAC at a dose of 20 mg daily due to atrial fibrillation.

4. Conclusion

Because of anticipated antiplatelet medication risks, patients who are not DES candidates or who are at particularly high risk for bleeding events have been targeted initially for treatment with the COBRA PzF Coronary Stent System. The particular patient described in this report is an ideal example of the intended clinical population for the COBRA PzF Stent and describes how the new stent design and materials serve this currently unmet clinical need. Because of various comborbid factors, stent selection was critical to the initial and long term clinical results seen with the COBRA PzF Stent. Planned clinical investigations of the stent are needed to establish the clinical utility of the device.

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Disclosure

The COBRA PzF Stent System is an investigational device and not approved for sale in the United States, however, it is available for sale in countries accepting CE marked devices.

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References


