CLINICAL RESEARCH

Immediate and 1-year follow-up with the novel nanosurface modified COBRA PzF stent

Résultats immédiats et à 1 an avec le stent COBRA PzF stent, à surface modifiée avec des nano-particules

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Summary
Background. — The COBRA PzF coronary stent, which has a unique nano-coating of Polyzene-F, was developed to reduce the risk of stent thrombosis.

Aims. — To report procedural and 1-year clinical outcomes following COBRA PzF coronary stent implantation in a real-world percutaneous coronary intervention (PCI) registry.

Methods. — All patients assigned to treatment with the COBRA PzF in the GCS Axium Rambot Center, Aix-en-Provence, France between February 2013 to June 2014 were prospectively enrolled.

Results. — Among 100 patients (71% men, mean ± standard error age 71.4 ± 11.0 years), 38% had acute coronary syndromes. The population was consistent with real-world experience and included patients with multiple co-morbidities and 26% with diffuse multivessel disease. A total of 151 lesions were treated with 166 stents, including 26% of lesions with a type B2 or C classification. Pre- and post-procedural quantitative coronary angiography analyses showed a mean

Abbreviations: BMS, bare-metal stent; CABG, coronary artery bypass graft; DAPT, dual antiplatelet therapy; DES, drug-eluting stent; NSTEMI, non-ST-segment elevation myocardial infarction; PCI, percutaneous coronary intervention; PzF, poly-bis(trifluoroethoxy) phosphazene; QCA, quantitative coronary angiography; SE, standard error; STEMI, ST-segment elevation myocardial infarction; TIMI, thrombolysis in myocardial infarction.

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One year results with COBRA PzF

Outcomes after percutaneous coronary intervention (PCI) have improved greatly since the introduction of stents [1–4]; and dual antiplatelet therapy (DAPT) [5] with P2Y12 inhibitors has been shown to significantly reduce abrupt stent occlusion. Subsequently, drug-eluting stents (DES) [6] reduced the need for repeat intervention by inhibition of neointimal hyperplasia [7]. However, DES safety concerns surfaced in real-world scenarios when higher rates of late stent thrombosis were noted compared with bare-metal stents (BMS) [8–10]. Late stent thrombosis is associated with high mortality [11] and may be a limitation for any technologies that inhibit healing, including bioreabsorbable DES [2,12–14]. Consequently, patients who receive DES require long-term DAPT, which increases both the cost and the risk of severe bleeding [15]. The latter is also associated with increased mortality [16,17]. The optimal duration of DAPT after DES implantation remains a matter of debate [18,19]. Furthermore, increasing numbers of patients require coronary revascularization and are at high risk of bleeding on DAPT (e.g. frail or elderly patients, those who require chronic oral anticoagulation, those awaiting urgent surgery, and those with major liver or kidney dysfunction or anaemia). In such patients, short-term DAPT treatment could reduce complications and enhance outcomes.

Work has therefore been undertaken to develop a DES with a lower risk of late stent thrombosis. Pre-clinical testing has demonstrated that a nano-thin coating of polybis(trifluoroethoxy) phosphazene (Polyzene-F or PzF) has a unique biocompatibility profile that is associated with preferential adsorption of albumin without denaturing or alteration to quaternary protein structures [20–27]. Rapid population of the stent surface with structurally intact albumin results in very low platelet and fibrinogen adhesion.
as well as reduced platelet activation and a rapid re-endothelialization. The biomimetic surface modification has been shown to reduce stent thrombosis and help prevent tissue reaction (inflammation) and restenosis [20–27].

The COBRA PzF (CeloNova Biosciences, San Antonio, Texas, USA) coronary stent has a new stent design: a balloon-expandable cobalt chromium alloy that is pre-mounted on a custom rapid-exchange balloon delivery catheter. The advanced alloy stent is polished and the surface is coated with a very thin nano-layer of PzF. COBRA PzF received CE mark (N CE 590539) in 2012. Using the COBRA PzF, we reported a complete reendothelialization within seven days in a rabbit iliac artery angioplasty model (unpublished data), which has been well correlated to human application [28].

Nevertheless, limited data are available on the effectiveness of COBRA PzF in routine medical practice. Therefore, it is important to assess the safety and effectiveness of the COBRA PzF coronary stent system in an everyday clinical setting. We report a prospective consecutive series of patients treated with COBRA PzF stents.

Methods

Study design

This study was performed in the GCS Axium Rambot centre, Aix-en-Provence, France, which undertakes approximately 1200 PCI procedures annually. The study population consisted of all patients who underwent PCI exclusively with the COBRA PzF stent between February 2013 and June 2014. All clinical indications were included, from stable angina to acute coronary syndromes, with a diverse range of lesion characteristics representative of a real-world cohort. Informed consent was obtained for all patients.

Baseline demographic characteristics were collected prospectively in a local database. The use of online quantitative coronary angiography (QCA) to assess appropriate device size was at the operator’s discretion. All angiographic films were reviewed to obtain procedural and angiographic characteristics. Pre- and post-procedural angiograms were analysed offline with QCA software. Patients received DAPT for one month after stent implantation. Clinical follow-up was obtained by telephone contact and a copy of electrocardiogram from the patient’s referring cardiologist, done at one month, six months and at one year, was collected and reviewed.

All reported events were verified and adjudicated by interventional cardiologists according to the criteria defined below.

Stent

The COBRA PzF stent system is a CE-marked new balloon-expandable cobalt chromium alloy stent with a modified thin strut open-cell design. The COBRA PzF stent with Polyzene-F features a rapid exchange delivery system and is available in 30 size variants ranging in diameter from 2.5 to 4.0 mm and lengths from 8 to 30 mm. The stent surface is coated with a nano-thin Polyzene-F layer: a permanent, ultrapure synthetic polymer.

QCA

Angiographic films were analysed with dedicated software (DFP-dedicated QCA algorithm: flat-panel analysis software, Version 4.1.13, GE Healthcare, Chalfont Saint Giles, UK) by two of the investigators. Reference vessel diameter, minimal luminal diameter and percentage diameter stenosis were obtained for the target vessel in the pre- and post-procedural angiographic film. Acute gain was defined as the absolute difference between pre- and post-procedure minimal luminal diameter.

Definitions

Angiographic success was defined as < 30% residual stenosis of the target lesion on QCA, with no residual thrombus and target vessel Thrombolysis In Myocardial Infarction (TIMI) grade 3 flow. Device success was defined as < 30% final residual stenosis of the target lesion using only the COBRA PzF.

Target vessel revascularization (TVR) was defined as any revascularization in the target vessel. Target lesion revascularization (TLR) was defined as any revascularization within 5 mm of the index lesion. Target vessel failure (TVF) was defined as a composite of all-cause mortality, myocardial infarction or target vessel revascularization. Target lesion failure (TLF) was defined as the combination of cardiac death, target vessel myocardial infarction (MI) or clinically driven TLR.

Procedural success was defined as angiographic success in the absence of in-hospital target vessel failure. Myocardial infarction definitions were in accordance with the most recent universal definition of myocardial infarction [29]. Stent thrombosis was defined according to the Academic Research Consortium definition [30].

Statistical analysis

All results are expressed as mean ± standard error (SE). Cumulative event rates were estimated using the Kaplan–Meier method. Follow-up was censored at 1 year. Statistical analysis was performed using SPSS version 20.0 (IBM Corp., Armonk, New York, USA).

Results

Baseline and lesion characteristics

One-hundred patients were enrolled and 151 lesions were treated. Baseline and lesion characteristics are shown in Table 1. The mean ± SE age was 71.4 ± 11.0 years, patients were predominantly male (71%), and 22% had diabetes. Stable angina was the most common indication for PCI (62%). Twenty-six patients had multivessel disease. Most lesions were type B1 while lesion types B2 or C (American Heart Association/American College of Cardiology classification) represented 26%, including two left main and 12 kissing stent bifurcation lesions.
Procedural characteristics

Procedural characteristics are shown in Table 2. In total, 166 stents were implanted. Pre-dilatation was performed for 82/166 stents (49.4%), rotational atherectomy in 6/151 lesions (4.0%) and thrombus aspiration in 10/151 (6.6%) lesions. Complete revascularization was achieved in all cases.

QCA

Baseline QCA analyses were available for all lesions (Table 3). Pre-procedural mean ± SE minimal luminal diameter was 1.0 ± 0.4 mm, with a mean diameter stenosis of 62.3%. Post-procedural mean ± SE minimal luminal diameter was 3.2 ± 0.4 mm, resulting in an acute gain of 2.2 ± 0.2 mm. Angiographic success was 100%.
Clinical outcomes

All patients were contacted at 1 month, 6 months and at 1 year (± 15 days); no patients were lost to follow-up. No in-hospital adverse events occurred (procedural success 100%). Two cases of cardiac death had occurred by 1-year follow-up (both cases are terminal cardiac insufficiency with renal dysfunction) (Table 4). Five patients had periprocedural myocardial infarctions (isolated troponin elevation without chest pain or Q waves) and five had target lesion revascularization. Overall, TVF occurred in 12 patients. No cases of stent thrombosis were observed.

Discussion

This systematic analysis of intermediate (one-year) outcomes with the COBRA PzF coronary stent included 100 patients treated with 166 devices. The study was an intent-to-treat design and included patients with complex anatomy or so called “all comers”, as reflected by the stent/patient ratio of 1.66. Further, all patients were referred to a tertiary high-volume centre. Acute successful stent implantation was achieved in 100% of patients with a significant (2.2 mm) acute gain. TLF was seen in 12% of patients at one year, driven by a 5% TLR rate and a 2% mortality rate and 5% of isolated troponin elevation at the time of procedure. These rates are better than those seen with other commercially available BMS in the United States [7,31,32]. The mortality rate observed in this study (2% at 12 months) is acceptable in this high-risk population. The two deaths were observed in elderly patients (83 and 92 years old) with severely impaired cardiac and renal function. No stent thrombosis was observed despite a high rate of comorbidities, the complexity of the lesions and the use of 1 month of DAPT. This registry provides some preliminary insights into the use of the study stent in patients with diabetes, bifurcation lesions, acute coronary syndromes, and elderly patients who are at high risk for bleeding on DAPT. These patients are becoming more common in daily practice as patients with stable coronary artery disease and simple coronary lesions are becoming a rarity.

The thrombosis-resistant coating of the study stent and the excellent one-year outcomes support further study, especially in patients at risk of bleeding. While the literature is replete with data suggesting the superiority of DES over BMS in routine practice [33], a significant proportion of patients still receive a BMS. One of the most frequent reasons for implanting a BMS is related to the need for only one month of DAPT whereas DES require 6–12 months [34,35].

There is a growing segment of the population, especially—but not exclusively—elderly or frail patients with non-documented anaemia, impaired renal dysfunction or atrial fibrillation that are at high risk of both thrombotic events and bleeding complications. Thrombosis of coronary stents is an infrequent but serious complication of PCI, and major bleeding is also associated with a higher rate of mortality [36]. Adding a P2Y12 receptor antagonist to low-dose aspirin has large benefits [37–39]. However, this strategy remains debatable in the high haemorrhage risk population.

A radial approach has reduced the risk of groin haematoma associated with the femoral route, and subsequently reduced procedural mortality [40,41]. However, there are still many situations where the duration of DAPT—especially when combined with anticoagulation therapy (e.g. atrial fibrillation, mechanical heart valve, recurrent deep-vein thrombosis)—needs to be as short as possible to limit the risk of haemorrhage. The COBRA PzF stent offers a potential alternative to current devices with a rapid and complete re-endothelialization, a low rate of repeat revascularization and restenosis, and the opportunity to reduce the DAPT period for this high-risk population. Therefore, until we have a DES that has a favourable efficacy (reduced restenosis) and safety (no stent thrombosis) with a short course of DAPT, there is a need for a stent with near-DES efficacy that does not require >2–4 weeks DAPT. The excellent acute and midterm results reported herein bring the DAPT strategies to the foreground. For many years, it seemed that longer DAPT was better than a single antiplatelet therapy post stent implantation, without any consensus on high bleeding risk populations. New guidelines could be considered, which depend on both haemorrhagic and thrombotic risks; and the COBRA PzF stent could become an alternative to the DES.

Limitations

This study has the limitations of a registry. This was a prospective single-centre study including 100 patients with no control group or randomization to compare the use of this device with contemporary devices. Selection biases have therefore occurred when determining which patients were suitable for the COBRA PzF stent implantation. Further, QCA
analyses were not performed by an independent core laboratory. Lastly, although clinical outcomes were obtained, no angiographic or other invasive imaging follow-up was systematically performed.

Conclusions

This single-centre registry reflects daily clinical practice in a high-volume centre, and included patients with high-risk lesions and significant co-morbidities. Our initial experience is very encouraging and suggests that the use of the COBRA PzF stent is safe and effective in a daily practice setting. Our results in this registry demonstrate successful acute performance and 1-year clinical outcomes. Large multicentre clinical studies would further validate and support these encouraging results in several specific indications.

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Disclosure of interest

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