Comparative study between Nano-surface Polyzene F and drug eluting stents in acute coronary syndrome patients with one-month dual antiplatelet therapy: Immediate and one-year clinical outcome.

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Comparative Study Between Nano-surface Polyzene F and Drug Eluting Stents in Acute Coronary Syndrome Patients with One-Month Dual Antiplatelet Therapy: Immediate and One-year Clinical Outcome

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Abstract

Background and objectives: The current clinical practice advocates dual antiplatelet therapy (DAPT) for a year after stent thrombosis (ST) segment elevation myocardial infarction (STEMI), primarily owing to persistent thrombotic risk. The novel COBRA PzF coronary stent was developed to reduce ST risk. The primary goal of the current research was to compare the efficacy and safety of the novel nanocoated PzF stenting with one-month DAPT against 12-month DAPT after the current drug-eluting stent (DES) in STEMI patients and single-vessel coronary artery disease (CAD).

Patients and methods: A prospective observational study enrolled 100 cases presented with STEMI and single vessel CAD. Eligible patients were allocated into 2 groups; group I consisted of 50 patients managed with the COBRA PzF stent who received one-month DAPT. Group II consisted of 50 patients treated with DES who received one-year DAPT. The occurrence of ST was our primary endpoint. The secondary endpoints were target vessel revascularization and major adverse cerebro-cardiovascular occurrences throughout the year.

Results: There were no observed cases of definite ST in group I against three in group II, however, it did not reach statistical significance ($P = 0.094$) The incidence of target vessel revascularization (6% against 10%), death (2% versus 4%), stroke (0 versus 2%) and major bleeding (0% versus 4%) observed in group I and II, respectively, however, it did not reach statistical significance.

Conclusion: The COBRA Polyzene-F stent with one-month DAPT met the performance goals for ST in patients presenting with STEMI with single vessel CAD and compared favorably with the commercially available DES with one-year DAPT.

Keywords: COBRA Polyzene F stent, Coronary artery disease, Drug eluting stent, Dual antiplatelet therapy, ST segment Elevation myocardial infarction, Stent thrombosis

1. Introduction

The American College of Cardiology (ACC)/ American Heart Association (AHA) and the European Society of Cardiology (ESC) advocate 12 months of DAPT following an acute coronary syndrome (ACS) incident for all patients, either treated conservatively or by percutaneous coronary intervention (PCI).[1,2] DAPT is required during the first months following stent implantation until re-endothelization becomes complete to avoid thrombosis of a device and restenosis in those patients who had been treated by PCI, who definitely represent a greater thrombotic risk subgroup.[3] The SMART-DATE study[4] enrolled 2712 participants who were receiving PCI for an ACS (NSTEMI/

NSTEMI/unstable angina). The patients were randomized into two groups based on DAPT duration into short-term 6 months group and to a longer duration 12-months group. All-cause mortality, myocardial infarction (MI), and stroke rates were the same in both study arms (4.7% versus 4.2%, respectively), but a significant increase in myocardial infarction has been observed in the short-term DAPT group, raising concerns about the safety of short DAPT treatment in patients with ACS. Drug-eluting stents have decreased in-stent restenosis; however, because of delayed vessel wall healing, a prolonged DAPT dual duration is required to mitigate stent thrombosis (ST). A shorter duration of DAPT may be a safe option with the COBRA PzF nanocoated coronary stent because it was linked to rapid endothelialization in comparison to DES, decreased inflammation, and thromboresistance.[5−7]

Our study's main goal was to compare the efficacy and safety of the novel nanocoated PzF stenting with one-month DAPT, then aspirin monotherapy, against 12-months of DAPT following the current drug-eluting stent (DES) in ACS/STEMI patients presenting with single vessel disease.

2. Patients and methods

Between October 2019 and June 2021, we conducted the current study, which was a prospective interventional study that enrolled 100 cases, presented by ACS/STEMI with documented single vessel coronary artery disease (CAD) requiring primary PCI. The patients were randomized and divided into 2 groups: group I consisted of 50 patients who underwent COBRA PzF stent treatment and received DAPT for one month, followed by antiplatelet monotherapy afterward. Group II consisted of 50 patients who were given commercially available second-generation drug eluting stents (Onyx Resolute, Xience Xpedition, or Ultimaster DES) and received DAPT for one year. Clinical follow-up was achieved for one year. Ethical approval was obtained from ethical committee at the pertained institutes.

2.1. Inclusion criteria

All comers ACS/STEMI patients with single vessel disease with no contraindication for PCI were enrolled in this study.

2.2. Exclusion criteria included patients with

(1) Patients presented with STEMI and multi vessel CAD.
(2) Previous stent anywhere within the target vessel.
(3) Previous coronary artery bypass surgery.
(4) Any contraindication for DAPT.
(5) Co-morbid disease with limiting life time expectancy as malignancy.

2.3. Medication protocol

Group A was given DAPT (Clopidogrel 75 mg and aspirin 100 mg) for one month post-PCI; the rest of the study involved antiplatelet monotherapy (100 mg of aspirin).

Group B was given DAPT for 12 months after PCI (clopidogrel 75 mg and aspirin 100 mg).

2.4. Endpoints

The incidence of ST was the primary endpoint of our research. The clinically determined incidence of target vessel revascularization, death, stroke, and major bleeding throughout the one-year clinical follow-up were the secondary endpoints.

2.5. Definitions

Acute ST was classified as happening within 24 h, subacute thrombosis as occurring between greater than 24 and 30 days, late thrombosis as occurring between greater than 30 days and one year, and very late thrombosis as occurring greater than 1 year. Early ST (acute and sub-acute) has been classified as happening within 30 days.[8] The term 'target vessel failure' (TVF) refers to a combination of cardiac mortality, target vessel MI, or recurrent revascularization of any target vessel segment. All fatalities that had no obvious noncardiac cause were assumed to be cardiac. MI has been classified as either Q-wave MI with new pathogenic Q waves and any rise of creatine kinase-MB (CKMB) or non-Q-wave MI if the CKMB rise was greater than three times the site-specific upper limit of normal or if the troponin rise was greater than three times the site-specific upper limit of normal in the absence of CKMB. Clinically driven TVR has been taken into consideration when functional ischemia study results were positive or when ischemic symptoms were present along with angiographic minimal luminal diameter stenosis of greater than or equal to 50% as defined by core laboratory quantitative coronary angiography (QCA) or revascularization of a target vessel with diameter stenosis of greater than or equal to 70% by QCA when neither angina nor a positive functional study result were present.[9,10]

2.6. Follow up

A copy of the patient's ECG taken at 1 month, 6 months, and 1 year was obtained from the patient's referring cardiologist and evaluated as part of the clinical follow-up.

2.7. Statistical analysis

All variables have been recorded, a descriptive analysis has been performed, and the data have been gathered in a particular format, confirmed, and then coded before the analysis as necessary. Unless otherwise stated, all continuous data are presented as mean ± SD, categorical data are presented as frequency in tables, and enumeration data are presented as case percentages and numbers.

The χ^2 test is used to evaluate associations in categorical data.

P values that are less than 0.05 are regarded as significant.

Nonparametric tests have been employed to determine the association between various variables.

All analyses were carried out using the Statistical Package for Social Sciences (SPSS) version 10 for Windows and MS Excel for graphics.

3. Results

3.1. Baseline characteristics

Baseline demographic characteristics presented in Table 1. Majority of the patients were men in both groups with no statistically significant differences noted regarding patients' age, hypertension, diabetes mellitus, dyslipidemia and smoking. Baseline ejection fraction was satisfactory in both groups, yet, significantly lowers in group II. Anterior STEMI was predominant in group I (60% versus 38%) while inferior STEMI was predominant in group II (40% versus 62%), however it didn't reach statistical significance.

3.2. Coronary angiography and percutaneous coronary intervention characteristics

Baseline procedural characteristics highlighted in Table 2. LAD was the culprit vessel in vast majority of patients in group I, while RCA was the culprit in group II ($P = 0.012$). Baseline TIMI Zero score denoting total culprit artery occlusion was significantly evident in group II (80% versus 90%, $P = 0.0001$), fortunately, post procedure TIMI III flow has been achieved in 100% of patients in both groups. Post stent dilatation, use of thrombus aspiration and intracoronary medications were similar in both groups. Immediate post primary PCI complications were not statistically different in both groups.

3.3. Clinical one-year outcomes

Baseline Clinical one-year outcomes depicted in Table 3. The primary endpoint of our research was the incidence of ST, this was dominant in group II complicating outcome in three patients but not in any patient in group I, despite the higher incidence, it did not statistical significance ($P = 0.094$). The occurrence of major adverse cerebro-cardiovascular incidents such as major bleeding, stroke, target lesion revascularization, myocardial infarction, and cardiac death were equally distributed in both groups with no statistical difference.

4. Discussion

4.1. Stent thrombosis incidence and effect of stent type

The results of the randomized trials show that the prevalence of ST and myocardial infarction is

Table 1. Baseline characteristics of studied groups.

Parameter	Group I (PzF stent)	Group II (DES)	P-value
Sex			
Male	35 (70%)	37 (75%)	0.661
Female	15 (30%)	13 (25%)	
Age/year	57.29 ± 8.4	58.14 ± 9.2	0.629
Hypertension%	29 (58%)	16 (32%)	0.016
Current smoker%	23 (46%)	21 (42%)	0.842
Diabetes mellitus%	14 (28%)	15 (30%)	1.0
Dyslipidemia%	33 (66%)	31 (62%)	0.838
Impaired GFR (glomerular filtration rate)	13 (26%)	13 (26%)	1.0
Ejection fraction (EF) %	56.37 ± 6.26	53.74 ± 6.96	0.048
Atrial fibrillation	0 (0%)	1 (2%)	0.369
Oral anti-coagulant	0 (0%)	1 (2%)	0.369
anterior STEMI	30 (60%)	19 (38%)	0.165
Inferior STEMI	20 (40%)	31 (62%)	0.167

Underline indicates $P < 0.05$ = Significant.

Table 2. Procedural characteristics.

Parameter	Group I (PzF stent)	Group II (DES)	P-value
Target vessel			
Left anterior descending (LAD)	30 (60%)	19 (38%)	0.012
Left circumflex artery (LCx)	6 (12%)	5 (10%)	
Right coronary artery (RCA)	14 (28%)	26 (52%)	
Baseline TIMI Zero score	40 (80%)	45 (90%)	0.0001
Aspiration	1 (2%)	0 (0%)	0.237
Intra-coronary medications	6 (12%)	4 (8%)	0.505
post-dilation	9 (18%)	6 (12%)	0.577
TIMI III post PCI	50 (100%)	50 (100%)	1.0
PCI complications	3 (6%)	4 (8%)	0.673

Underline indicates $P < 0.05$ = Significant.

Table 3. Clinical one-year outcomes.

Parameter	Group I (PzF stent)	Group II (DES)	*P*-value
Stent thrombosis	0 (0%)	3 (6%)	0.094
Major bleeding	0 (0%)	2 (4%)	0.094
Stroke	0 (0%)	1 (2%)	0.237
target vessel revascularization (TVR)	3 (6%)	5 (10%)	0.214
Cardiac Death	1 (2%)	2 (4%)	0.554
Net adverse cardiovascular events	4 (8%)	7 (14%)	0.55

Underline indicates $P < 0.05$ = Significant.

significantly lower with extended DAPT than with shorter DAPT for up to 36 months after DES, with relative risk reductions of 50% and 35%, respectively. However, there is a lack of information on COBRA PzF's efficacy in standard medical practice. As a result, it was critical to evaluate the COBRA PzF coronary stent system's safety and efficacy in a daily clinical setting Tamburino and colleagues.[7] In the current investigation, the ST rate has been unnoticed in group I (COBRA stent) and complicated the course of group II in three patients (6%). At one year, the incidence of ST in the DES group with STEMI was comparable to that reported in various modest-sized randomized studies comparing DES to bare metal stents, which ranged from ≈1%3 to as high as 3−4% Valgimigli and colleagues[11] and Donald and colleagues.[12] However, the rate of ST after STEMI was significantly higher than the 0.1%−0.6% early rates of ST observed in randomized controlled studies of DES in patients with stable coronary artery disease, as well as the 1.5% early rates of ST observed in the Acute Catheterization and Urgent Intervention Triage Strategy (ACUITY) study in moderate- and high-risk patients with non-STEMI Spaulding and colleagues.[13] The thromboresistant and pro-healing qualities of the polymer Polyzene F-coated (COBRA PzF) stent, may safely permit for a very short period of DAPT; these are the main factors underpinning the prevention of ST (both early and late) in group I. Our results are comparable with those of Koppara et al., who indicated that the Cobra Stent's thin, flat struts exhibit a decent ST/TVR and provide a good option for patients who need a short DAPT Brar and colleagues.[14] They are covered with a nano-layer of PzF to promote speedy healing and provide thrombo-resistant properties Aoki and colleagues.[15] The lack of ST in our investigation is consistent with results from preclinical studies, which demonstrated significantly decreased platelet adhesion and thrombogenicity for stents coated with a nano-layer of PzF. There have only been two sub-acute ST occurrences

and no late ST to date among the published outcomes involving more than 650 patients who had either the Catania or COBRA PzF stent. It ought to be emphasized that the findings of our research show that more than 50% of subjects were still receiving DAPT at 9 months Nso and colleagues.[16]

4.1.1. Bleeding risk and one-month versus 12-months DAPT in both groups

In ACS patients with single vessel disease, our study compared the efficacy and safety of stopping DAPT at one month in PzF COBRA stents to 12-months DAPT in patients undergoing PCI with conventional DES. When compared with 12-month DAPT, one-month DAPT with aspirin monotherapy was related to identical ischemic results and lower hemorrhage among participants who adhered to therapy and were free of ischemic occurrences throughout the first month post-PCI. Because of a shorter DAPT interval in group I, it was not surprise that major bleeding was actually reduced following treatment with PzF-stent however, it did not reach the statistical significance (0% versus 4%; $P = 0.094$). The demonstrated less bleeding benefit despite it did not reach a statistical significance was associated with a similar ischemic event compared with one-year in patients who received DES. Both treatment arms were practically identical in demographic, procedural and post-procedural regimens.

4.1.2. Target vessel revascularization during periprocedural period through 12-month clinical follow-up

A re-intervention motivated by any lesion in the same coronary artery is referred to as 'target vessel revascularization' (TVR), and it may involve a coronary artery bypass graft that involves infarct related artery. In the current investigation, groups I and II had relatively low rates of clinically driven TVF (6% versus 10%, $P = 0.214$ respectively). This outcome is congruent with preclinical investigations that reveal the COBRA PzF stent with a PzF surface modification to have reduced neointimal response, reduced inflammation, and enhanced healing when compared with other BMS and second-generation DES. Nonetheless, the obtained results are comparable to previous published literature Koppara and colleagues.[17]

The relatively limited number of TVF could be related to many factors. It is a balloon-expandable, thin-strut stent (71 μm), and most notably, the pro-healing characteristics of the COBRA PzF could suppress atherogenicity while reducing neointimal hyperplasia. In-stent restenosis is

caused by myointimal damage, neointimal hyper-plasia, vascular remodeling, and elastic recoil in PCI settings. Osteal lesions, vascular caliber, and genetic predisposition are additional risk factors for in-stent restenosis and later ST. In terms of safety and efficacy, contemporary second-generation DES outperform early-generation stents in patients undergoing percutaneous coronary intervention, thanks in part to thinner struts that result in better clinical results when compared with older, thicker struts.

4.1.3. Major adverse cardiac events and one-year follow-up

At 30 days, the primary endpoint of early (acute and subacute) ST happened in two cases in the DES group, or 2% of the patient population, and cardiac death occurred in one patient during the hospital course after an attack of VT following anterior STEMI and primary PCI with a DES.

Clinical events at one-year are shown in Table 3. The COBRA-PzF stent is effective and safe in routine practise as it reduces the likelihood of ST by shortening the duration of DAPT to one month and has the potential to lower bleeding risk, which is crucial for patients with high bleeding risk. The net adverse cardiac events have been similar in both groups. Large multicenter clinical investigations would confirm and validate these optimistic findings for a number of particular indications.

4.2. Limitations of the study

There are many limitations of the current study; one of the most important of them is small number of patients as well as being a non-randomized study. The clinical outcome based primarily on history taking and clinical examination, coronary angiographic was limited to those patients who presented with ST.

4.3. Conclusion

The COBRA PzF stent met the preestablished performance objectives for both the primary endpoint of ST and the supported secondary endpoints of safety and efficacy issues. As far as we are aware, this research was the first to address the topic of one-month DAPT in STEMI patients. Further large-scale trials are highly recommended to confirm our results for proper patients' longevity.

Conflicts of interest

None declared.

References

1. Valgimigli M, Bueno H, Byrne RA, et al. ESC focused update on dual antiplatelet therapy in coronary artery disease developed in collaboration with EACTS: the task force for dual antiplatelet therapy in coronary artery disease of the European Society of Cardiology (ESC) and of the European Association for Cardio-Thoracic Surgery (EACTS). *Eur J Cardio Thorac Surg*. 2018;39:213−260.
2. Amsterdam EA, Wenger NK, Brindis RG, et al. AHA/ACC guideline for the management of patients with non- ST-elevation acute coronary syndromes: a report of the American College of Cardiology/American heart Association task force on practice guidelines. *J Am Coll Cardiol*. 2014;64:e139−e228.
3. Verdoia M, Sartori C, Pergolini P, et al. Prevalence and predictors of high-on treatment platelet reactivity with ticagrelor in ACS patients undergoing stent implantation. *Vasc Pharmacol*. 2016;77:48−53.
4. Hahn J-Y, Song YB, Oh J-H, et al. 6-month versus 12-month or longer dual antiplatelet therapy after percutaneous coronary intervention in patients with acute coronary syndrome (SMART-DATE): a randomised, open-label, non-inferiority trial. *Lancet*. 2018;391:1274−1284.
5. Cornelissen A, Sakamoto A, Sato Y, et al. COBRA PzF™ coronary stent in clinical and preclinical studies: setting the stage for new antithrombotic strategies? *Future Cardiol*. 2022;18: 207−217.
6. Stampfl U, Sommer CM, Thierjung H, et al. Reduction of late in-stent stenosis in a porcine coronary artery model by cobalt chromium stents with a nanocoat of polyphosphazene (Polyzene-F). *Cardiovasc Intervent Radiol*. 2008; 31:1184−1192.
7. Tamburino C, Capodanno D, Di Salvo ME, et al. Safety and effectiveness of the Catania Polyzene-F coated stent in real world clinical practice: 12-month results from the ATLANTA 2 registry. *EuroIntervention*. 2012;7:1062−1068.
8. Martin K, Petr W. Stent thrombosis in acute coronary syndromes: patient-related factors and operator-related factors. *Anatol J Cardiol*. 2020;24:274−279.
9. Geyer M, Wild J, Hirschmann M, Zisis D, et al. Predictors for target vessel failure after recanalization of chronic total occlusions in patients undergoing surveillance coronary angiography. *J Clin Med*. 2020;9:178.
10. Byoung G, Seung W, Seong G, Cheol U, Min W, Suhng W. Association of major adverse cardiac events up to 5 Years in patients with chest pain without significant coronary artery disease in the Korean population. *J Am Heart Assoc*. 2019;8:e010541.
11. Valgimigli M, Campo G, Percoco G, et al. Comparison of angioplasty with infusion of tirofiban or abciximab and with implantation of sirolimus-eluting or uncoated stents for acute myocardial infarction: the MULTISTRATEGY randomized trial. *JAMA*. 2008;299:1788−1799.
12. Cutlip DE, Garratt KN, Novack V, Mark B, et al. 9-Month clinical and angiographic outcomes of the COBRA Polyzene-F NanoCoated coronary stent system. *JACC Cardiovasc Interv*. 2017;10:160−167.
13. Spaulding C, Henry P, Teiger E, et al. Sirolimus-eluting versus uncoated stents in acute myocardial infarction. *N Engl J Med*. 2006;355:1093−1104.
14. Brar SS, Leon MB, Stone GW, et al. Use of drug-eluting stents in acute myocardial infarction: a systematic review and meta-analysis. *J Am Coll Cardiol*. 2009;53:1677−1689.

15. Aoki J, Lansky AJ, Mehran R, et al. Early stent thrombosis in pa-tients with acute coronary syndromes treated with drug-eluting and bare metal stents: the Acute Catheterization and Urgent Intervention Triage Strategy trial. *Circulation*. 2009;119:687−698.

16. Nso N, Mahmoud N, Milana Z, Yolanda M, Anthony L, et al. Factors impacting stent thrombosis in patients with percutaneous coronary intervention and coronary stenting: a systematic review and meta-analysis. *Cureus*. 2022;14: e23973.

17. Koppara T, Sakakura K, Pacheco E, et al. Preclinical evalua-tion of a novel polyphosphazene surface modified stent. Koppara Preclinical testing of a PzF-coated stent. *Int J Cardiol*. 2016;222:217−225.