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The Usability, Safety, Efficacy and Positioning of the Atlas Drug-Eluting Coronary Stent: Evaluation the Preliminary Perioperative Results

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Research Article

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ABSTRACT

Background: Coronary Artery Disease (CAD) is the most common type of heart disease. For its revascularization, minimally invasive techniques have been the preferred treatment modality for the past two decades. However, restenosis is a significant issue after these techniques. Drug-Eluting Stents (DES), primarily sirolimus or paclitaxel- releasing, have started to be widely used to reduce the rate of restenosis.

Methods: 30 patients, 51-83 years old, who demonstrated significant coronary artery stenosis, were treated with the ATLAS Drug Eluting Coronary Stent System (AtlasPTCA®; Invamed, Ankara, Turkey) at the Medical Simulation and Training Center, MU Plovdiv, Bulgaria. Accurate positioning of the stent, which contains radiopaque tungsten-tantalum markings at the tips, was traced by angiographical imaging. Measurements of vessel sizes before and after treatment were performed using Quantitative Coronary Assessment (QCA). Quantitative analysis was performed by comparing the diameter of the reference vessel. Data were analysed using IBM SPSS statistical package version 25 program.

Results: After treatment, the final lumen diameter value was 3.45 ± 0.56 mm, similar to the diameter measurement of the reference vessel. Restenosis was not observed in any of the patients. No serious side effects are observed.

Conclusion: AtlasPTCA® is feasible and associated with a favourable profile of safety, efficacy, deliverability, and usability. Therefore, its use can provide a valuable aid in the treatment of coronary artery disease. For long-

term evaluation, more studies are needed.

Keywords: Coronary Artery Disease (CAD); Atlas drug-eluting coronary stent; AtlasPTCA®; Sirolimus-releasing; Radiopaque markers; Positioning

INTRODUCTION

The most common type of heart disease is Coronary Artery Disease (CAD), in which the arteries cannot deliver enough oxygen-rich blood to the heart due to plaque buildup in their walls [1]. Despite advances in diagnosis and treatment, it remains the leading cause of mortality and morbidity worldwide [2]. Coronary Artery Bypass Grafting (CABG), which is more invasive than Percutaneous Coronary Intervention (PCI), was the only revascularization therapy prior to the introduction of PCI in 1973. However, CABG is even superior in certain patient groups, and minimally invasive techniques have become the preferred method for revascularization in recent decades. Because the survival rate of patients with CAD has increased with PCI [2-5]. On the other hand, reocclusion after PCI has been a significant problem [6,7]. Re-occlusion may be due to acute thrombotic occlusion of a coronary artery or to Neointimal Hyperplasia (NIH) over a period of several weeks [8-10]. Restenosis requires PCI or CABG intervention to achieve revascularization [11]. Many factors are involved in the NIH process, including Smooth Muscle Cell (SMC), migration, extracellular matrix formation, and neutrophils/macrophages recruitment [12]. In the etiology of restenosis, patient-related factors (age, diabetes mellitus, genetics, etc.), lesion-related factors (type, length, location of the lesion, arterial size, etc.), procedural factors (type, length, expansion size, number of stents, positioning etc.) play role [13]. Drug-Eluting Stents (DES), which primarily releases sirolimus or paclitaxel, is now widely used to reduce the rate of restenosis [10]. These stents are usually made of metal such as stainless steel or cobalt chrome alloy [14]. Sirolimus blocks the action of mitogenic stimuli on cells by inhibiting the mammalian target of rapamycin complex 1 (mTORC1), a multiprotein complex that regulates cell proliferation [15]. The accurate positioning of the stent remains a major challenge in clinical practice. Stent disposition is around 1/3 of PCI procedures and has been associated with the number of stents placed per procedure, overlapping stents, increased target vessel revascularization, myocardial infarction, thrombosis in the stent, and death. They can be longitudinally, usually depending on technical failure that can result in edge lesions or axial, often depend on a design/ concept failure that potentially leading to in-stent lesions. The positioning inaccuracy can be longitudinal due to technical failure, which can often lead to edge lesions, or axial due to a design/concept error with the potential to cause in-stent lesions [16]. ATLAS Drug Eluting Coronary Stent System (AtlasPTCA®; Invamed, Ankara, Turkey), is a sirolimus-releasing balloon-expandable stent delivery system designed with laser cut biodegradable polymer layers. Its make-up also contains radiopaque markings of tungsten-tantalum-made at the tips, which allow for accurate positioning with a better traceability via imaging methods. The full details of the stent system are shown in Table 1.

Table 1. Characteristics of the ATLAS drug-eluting coronary stent system.

Characteristics	Values
Stent diameter	2-5 mm
Stent length	8-40 mm
Stent type	316 L Stainless steel
Catheter diameter	5F

Catheter length	140 cm
Guidewire compatibility	0.01
Stent-loaded RBP	20 atm between 2.00–5.00 mm
Stent-loaded NP	10 atm between 2.00–5.00 mm
Balloon deflating time	Less than 1 minute
Polymer	PLGA
Medicine	Sirolimus
amount of drug	1 µg+/-0,2/mm^2
Vessel diameters	Smaller vessel diameters of 0.2 mm to 0.3 mm per stent
Maximum size of stents to be used	Stents of different sizes up to 30 mm can be used Stents of different sizes up to 30 mm can be used Stents of different sizes up to 30 mm
Abbreviations: RBP: Rated Burst Pressure; NP: Nominal Pressure; PLGA: Poly (Lactic Acid-Coglycolic Acid)	

The objective of this study was to evaluate the first clinical results of the AtlasPTCA® stent, which was produced with laser cutting methods with greater compatibility with open-cell design technology, as well as to improve the lumen diameter in the stent and reduce restenosis at the edges of the stent in natural coronary arteries.

MATERIALS AND METHODS

Study design

This single-arm prospective study was conducted in a single center by a single cardiologist who has experience with coronary interventions. The PCI procedure was performed according to the standard of care. The placement of the stent was evaluated by angiographic methods. The patients were followed up by direct observation during their hospitalization and by telephone one week after discharge. User feedback was received through a questionary and all safety-related events were documented. In all patients, the placement of the stent was evaluated by angiographic images.

Ethical approval statement: The ethics approval committee for the study is the Ethics Committee of the Research Institute of Plovdiv Medical University, Bulgaria.

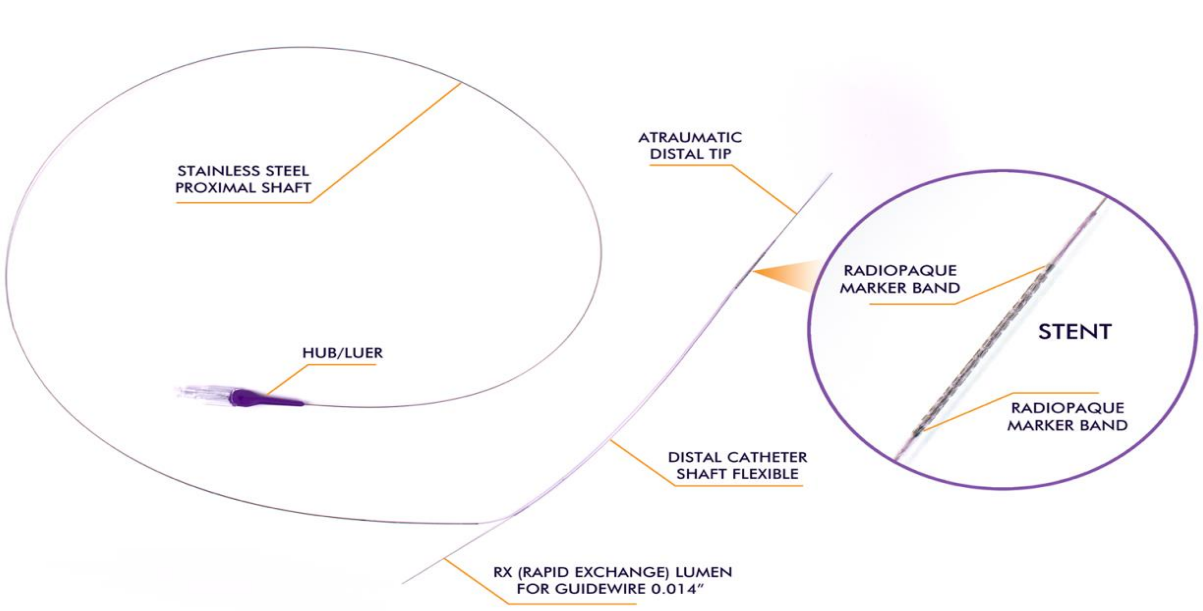
Patients: Patients aged at least 18 years who demonstrated significant coronary artery stenosis on coronary angiogram and met all inclusion and exclusion criteria were considered eligible for this study. Written informed consent was obtained from all eligible participants. Patients aged <18 years and with at least one clinically significant coronary stenotic lesion were eligible for PCI. Exclusion criteria did not apply to the type of lesion (bifurcation, ostial, and end-to-end lesions), the number of stents used, and the number of lesions treated. Patients with unstable hemodynamics, apparent intravascular thrombosis, and history of bleeding diathesis, known hypersensitivity or contraindication to anticoagulants or sirolimus were excluded from the study.

Evaluation of usability and safety: Usability and risks with usage errors were evaluated according to international standards, EN 62366-1:2015/AC-EQV; IEC 62366-1:2015/COR1-EQV. In this regard, dimensional verifications according to ISO25539 within the usability procedure, profile diameter tests, push ability, torque, balloon inflation and deflation time, burst pressure, balloon fatigue, stent diameter according to balloon inflation pressure, rebounding, crush resistance with radially applied load, flexing, bending, and balloon stent. Based on the anatomical characteristics of the lesions, the PCI stenting technique was considered usable when the appropriate

positioning of the stent was achieved. Any adverse medical events in a study subject were defined as Adverse Events (AE). A Serious Adverse Event (SAE) was defined as any adverse medical event that results in death, life-threatening, requiring hospitalization, or prolonged hospital stay. Device-related AE and SAE during hospitalization were the primary safety endpoint.

Study device and stenting: As shown in Figure 1, AtlasPTCA® has a simple structure that allows precise positioning on coronary lesions. Coronary angiography and consecutive coronary angioplasty were performed according to the established local protocol with small variations depending on the clinical scenario–urgent or elective procedure. All patients were consciously sedated with short-acting benzodiazepines, 2 mg of Midazolam or 2.5 mg of Diazepam IV. The access site was traditional right radial and the artery was punctured after application of 1-2 ml of 1% Lidocain locally. After successful puncture of the artery, a 6-French conventional sheath was inserted. The intervention was performed with a 6-French guiding catheter, chosen according to the affected artery (LCA/ RCA) and the complexity of the target lesion. Initially, a selected coronary guidewire was passed through the lesion and the stenosis was optimally predilated with a coronary balloon, corresponding to the size of the artery.

Figure 1. Schematic demonstration of the ATLAS drug-eluting coronary stent system.



After diligent preparation of the lesion, AtlasPTCA® was inserted and expanded at or above its nominal pressures up to the given rated burst pressures. Finally, the stent is postdilated with a non-compliant balloon sized according to the guidelines. Periprocedural pharmacotherapy includes heparin with a dose adjusted to the body weight of the patient and a loading dose of antiplatelet agents. Measurements of vessel sizes before and after treatment were performed using Quantitive Coronary Assessment (QCA). The minimum lumen diameter was measured within the stent and within the 5 mm proximal and distal edges of the stent. Quantitative analysis was performed comparing the reference vessel diameter.

Statistical analysis: Data were analyzed using IBM SPSS statistical package version 25 program. All data were summarized descriptively. Mean, standard deviation, median, and min-max values were used in the statistical

evaluation of continuous data, while frequency and percentage values were used in the definition of categorical variables.

RESULTS

In this single-center, single-operator study in Bulgaria, a total of 30 patients participated in the study. Most of the patients 80% were male. The mean age was 65.1 ± 7.9 (51-83) years. The 30 patients (100%) had Hypertension (HT) and 29 (96.7%) had Hyperlipidemia (HL). Ten (33.3%) had Diabetes Mellitus (DM) and 14 (46.7%) had a history of Myocardial Infarction (MI). Other baseline characteristics and clinical data are presented as shown in Table 2.

Table 2. Baseline characteristics of the patients (n: 30).

Variables	Percentage
Age (Years) ± SD	65.1 ± 7.9 (51-83)
Gender (F/M)	6/24 (20/80%)
DM	10 (33.3%)
HT	30 (100%)
HL	29 (96.7%)
Smoking	12 (40%)
Previous MI	14 (46.7%)
Previous CABG	1 (3.3%)
Previous PCI	20 (66.7%)
Lesion length (mm)	
Mean ± SD	27.67 ± 8.89
Median (Min-Max)	31(10-39)
Number of diseased arteries	
1	3 (10%)
2	8 (26.7%)
3	19 (63.3%)
Angiographic characteristics	
Target artery	
LAD	15 (50%)
LCx	6 (20%)
RCA	9 (30%)
Bifurcation lesion	17 (56.7%)
Ostia lesion	7 (23.3%)
Non-bifurcational and non-ostial lesion	6 (20%)
Pre-intervention drug therapy	
Aspirin	2 (6.7%)
Clopidogrel	22 (73.3%)
Prasugrel	5 (16.7%)
Ticagrelor	1 (3.3%)
Post-intervention drug therapy	
Clopidogrel	22 (73.3%)
Prasugrel	6 (20%)
Ticagrelor	2 (6.7%)
Treated coronary segment localization	
Proximal	9 (30%)
Middle	15 (50%)
Distal	6 (20%)
Overlapping Stent	3 (10%)

Abbreviations: LAD: Left Anterior Descending Artery; LCx: Left Circumflex Artery; RCA: Right Coronary Artery, SD: Standard Deviation

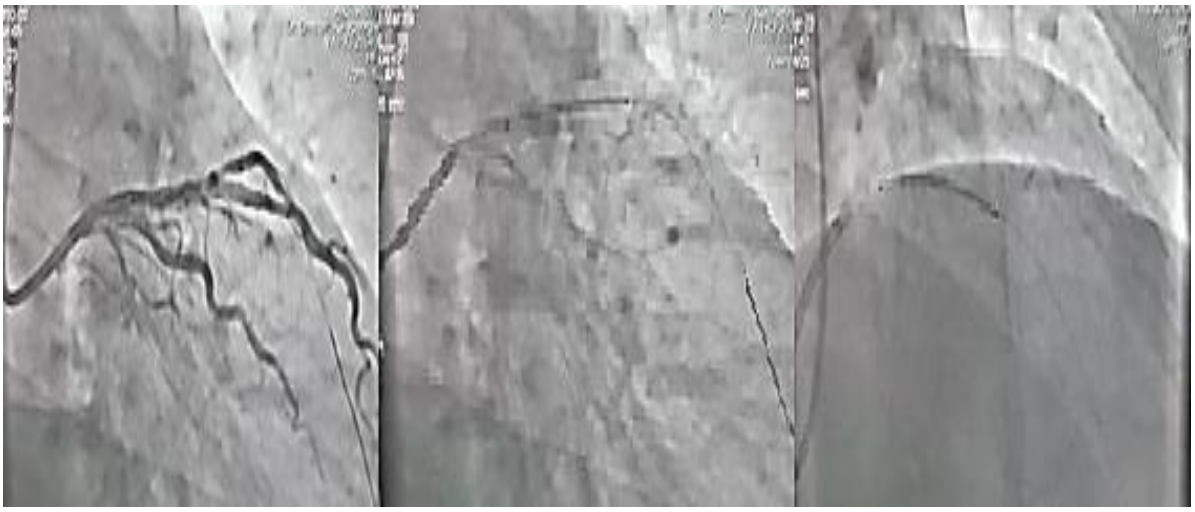
The mean and deviation of the final lumen diameter value was 3.45 ± 0.56 mm, similar to the measurement of the diameter of the reference vessel in Table 3. Restenosis was not observed in any of the patients, which means that the interventional success was found to be 100%.

Table 3. Angiographical characteristics of the vessels after treatment.

Size characteristics	Mean ± SD	Median (Min-Max)
Stent diameter	3.29±0.5	3.5(2.25-4.5)
Stent length (mm)	30.07±8.86	34(12-40)
Reference vessel diameter (mm)	3.45±0.56	3.58(2.3-4.7)
Final lumen diameter (mm)	3.45±0.56	3.58(2.3-4.7)

As a safety precaution, no serious side effects such as allergic reactions, aneurysms, thrombosis, arterial wall dissection, blood loss, death, recurrent vascular occlusion/spasm, and the urgent need for CABG/PCI were observed in any of the patients as shown in Figure 2.

Figure 2. Representative representation of the precise positioning of AtlasPTCA® with the aid of proximal and distal radiopaque markers on angiographic image.



DISCUSSION

Minimally invasive techniques are the preferred treatment modality for revascularization in CAD [2,3]. Restenosis, on the other hand, remains a challenge [6,7]. Patient-related factors (age, diabetes mellitus, genetics, etc.), lesion-related factors (type of lesion, length, location, arterial size, etc.), procedural factors (type, length, enlargement size,

number of stents, etc.) play a role in the etiology of restenosis [13]. DES has significantly improved clinical outcomes in coronary artery stenosis [14].

These stents offer different platforms and have advantages and disadvantages over each other. Some features, such as radial strength, reduced risk of recoil, and thin struts, provide optimum advantages for stents. For example, thinner struts are associated with lower rates of stent restenosis, thrombosis, and other side effects [17]. In this context, radiopaque markers also minimize procedural factors that would cause restenosis.

The unmet needs for precise positioning of the stent in the coronary artery led to several inventions for optimal intervention [14-16]. Due to the radiopaque markings of tungsten-tantalum made at the tips, AtlasPTCA® allows precise positioning of the stent over the lesion in the coronary artery. Furthermore, AtlasPTCAR also has distinctive properties such as high resistance to pressure and very short balloon deflating time with less than 1 min. It easily adapts to the arterial wall and does not dislodge after placement.

An ideal stent should have good biocompatibility, flexibility and deliverability, strong radial force, and good radiopacity under fluoroscopy. Again, in addition to providing effective revascularization, it should be safe, that is, it should result in a low rate of thrombogenesis, neointimal hyperplasia, and stent thrombosis in long-term follow-up [18]. Among the notable features of AtlasPTCAR, increased flexibility, superior adhesion to the arterial wall, as well as a ground-breaking radial force optimized to reduce thrombosis and neointima hyperplasia occur.

The biodegradable and biocompatible poly (lactic acid-coglycolic acid) (PLGA) polymer is widely studied for the controlled delivery of various drugs 5. The PLGA layer of the AtlasPTCA® stent is coated with sirolimus. These polymer layers release the sirolimus drug in a time-controlled process, maximized at 8 weeks, which steadily dissipates, ultimately preventing the formation of neointima in the stent. Effectiveness is one of the most important criteria for an ideal stent, the other two being safety and deliverability [18]. Regardless of the type of lesion (including bifurcational, ostial or other types of lesions and proximal, distal, or middle segmental lesions), it was observed that the diameters of the vessels of all patients reached the diameter of the reference vessel after treatment in our study. As an indicator of usability, the AtlasPTCA® stent is also easy to use and reliable. It reduces stenting time, even in a tortuous vessel. Inhibition of platelet activation is the main point of secondary protection after DES implantation.

CONCLUSION

Therefore, antiplatelets should be used to prevent stent thrombosis and avoid the risk of excessive bleeding, and the type and duration of the strategy should be tailored to the patient and the procedural characteristics. In conclusion, this prospective study demonstrates that the Atlas sirolimus eluting stent is feasible and associated with a favorable profile of safety, efficacy, deliverability and usability, which are characteristics of the ideal stent. Therefore, its use can provide a valuable aid in the treatment of coronary artery disease. The biodegradable nature of the polymer can be expected to yield superior results in relation to the incidence of in-stent thrombosis.

STUDY LIMITATIONS

This study evaluating the AtlasPTCA® stent has some limitations. The sample size was relatively small and the study was performed by a single center and by the same surgeon. The usability, safety, efficacy, and positioning of AtlasPTCAR were evaluated based on the results of the perioperative period. However, while we believe that these assessments shed light on longer-term results, there is no short, medium, or long-term assessment. The study also did not have a control arm.

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CONFLICT OF INTEREST

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CONTRIBUTIONS OF AUTHORS

OA conceptualized the article, analyzed, and curated the data. AFA searched the literature and drafted the manuscript. OA edited and supervised. All authors have read and agreed to the final version of the manuscript.

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