

## Early Outcome after Bioresorbable Vascular Scaffold Implantation in Patients with Acute Coronary Syndrome



### Healthcare

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### Abstract

The term acute coronary syndrome (ACS) refers to any group of clinical symptoms compatible with acute myocardial ischemia and includes unstable angina (UA), non-ST-segment elevation myocardial infarction (NSTEMI), and ST-segment elevation myocardial infarction (STEMI). These high-risk manifestations of coronary atherosclerosis are important causes of the use of emergency medical care and hospitalization. High-risk patients with UA/NSTEMI are often treated with an early invasive strategy involving cardiac catheterization and prompt revascularization of viable myocardium at risk. Transradial approach has important impact in reduction of bleeding and vascular complications. We evaluated the feasibility and the acute performance of the everolimus-eluting bioresorbable vascular scaffolds (BVS) for the treatment of patients presenting with ACS. Methods and results: The present investigation was a prospective, single-centre study, reporting data after BVS implantation in patients presenting with ACS. Clinical outcomes were reported at the 30-day, 6-month, 1 year and 2 years follow-up. Quantitative coronary angiography and optical coherence tomography (OCT) data were also evaluated. The intent-to-treat population comprises a total of 21 patients. The procedural success was 100.0%. In 14 patients (66.7%) BVS were implanted on left anterior descending artery (LAD), 4 patients (19.0%) on right coronary artery (RCA), 3 patients (14.3%) on circumflex artery (Cx). Pre-procedure TIMI-flow was 0 in 8 patients (38.1%). After the BVS implantation a TIMI flow 3 was achieved in all 21 patients and the post-procedure percentage diameter stenosis was 16.7 +/- 8.9%. No patients had angiographically visible residual thrombus at the end of the procedure. OCT analysis was performed in 13 patients (61.9%) showed that the post-procedure mean lumen area was 7.88 +/- 1.84 mm<sup>2</sup>, minimum lumen area 5.52 +/- 1.59 mm<sup>2</sup>. At the 30-day, 6-month, 1 year (15 patients) and 2 years follow-up (8 patients) target-lesion failure rate was 0%. Non-target vessel revascularization and target vessel myocardial infarction (MI) were not reported. No cases of cardiac death or scaffold thrombosis were observed. Conclusion: BVS implantation in patients presenting with ACS appeared feasible, with high rate of final TIMI-flow III and good scaffold apposition. Larger studies are currently needed to confirm these preliminary data.

### Introduction

Coronary artery disease (CAD) is defined as myocardial ischemia as a result of irregularity between oxygen supply and needs in myocardium (less supply and/or more need). Obstructive coronary arteries are the most common reason (90-95%) and rarely some congenital anomalies, inflammation process, embolisation, systemic diseases (arteritis, systemic lupus erythematosus).<sup>1</sup> Its epidemic character in last few decades is characterized with high morbidity and mortality especially with high prevalence in developing countries, expecting to widespread in develop countries in 2020 year. According to World Health Organization it is leading cause for mortality all around the world among the people aged 60 and older. Patients with CAD have stenotic or occluded coronary arteries, resulting with chest pain, shortage of breath in rest or during exercise, electrocardiographic changes, heart attack or death.<sup>2</sup>

CAD is characterized with variety of risk factors which can be defined as controlled and uncontrolled. Most common correlation is incidence of CAD with older age.<sup>3,4</sup> But things are changing, moving towards younger population aged 45 and less exposed to higher risk for CAD especially in developing countries.<sup>5,6</sup>

Acute coronary syndrome (ACS) is one of the most difficult clinical manifestation of CAD, continuing to be a major health problem, despite of impressive improvements in its diagnosis and therapy in last few decades. Because of the fact that a lot of population capable for working suffer from ACS, it is serious social and economy problem.<sup>7</sup> Widespread use of aspirin and percutaneous coronary interventions (PCI) result in decreasing of morbidity and mortality of ACS.<sup>8</sup>

Percutaneous coronary intervention (PCI) is an optimal strategy to re-open the occluded or significantly narrowed coronary artery (culprit vessel) and improve the outcomes of patients with ACS.<sup>9</sup> Access-site selection is an important procedural issue in PCI. Transradial approach (TRA) has been associated with lower rate of

access-site bleeding and vascular complications in comparison with transfemoral approach. This has been evident with the aggressive use of antithrombotic and antiplatelet therapy in patients with ACS.<sup>10</sup> Vascular access-site complications have been shown to be associated with worse outcomes.<sup>11</sup>

Bioresorbable vascular scaffold (BVS) is interventional percutaneous device for treatment of coronary artery disease (**Figure 1**). It is covered with bioresorptive polymer and cytostatic drug which is eluted in the coronary artery wall in the period of 1-2 months, preventing the uncontrolled neointimal hyperplasia. BVS introduction is the 4-th revolution in percutaneous coronary interventions after introducing balloon angioplasty in 1977, bare metal stents in 1988 and drug eluting stents in 2001 year.

## Methods

**Study population.** Patients with ACS scheduled for PCI and stenting regardless to indication were eligible to be included in this prospective study. The study is conducted in accordance with our local internal review board regulations and written informed consent was obtained from all patients prior procedures. Intention to be treated are 100 consecutive patients with ACS.

**Study protocol.** Patients were divided in two groups:

**Group 1** – consisting of 50 patients with ACS, with PCI through transradial approach and BVS implantation (Absorb Bioresorbable Vascular Scaffold System, Abbott Vascular);

**Group 2** - consisting of 50 patients with ACS, with PCI through transradial approach and second generation DES implantation.

**Vascular access.** The radial artery was accessed after local infiltration with 1-1.5 ml 2% lidocaine, using puncture technique with a 20 G plastic intravenous cannula and 0.025” mini guidewire (45cm) and followed by 5 Fr or 6 Fr hydrophilic introducer sheath (Terumo corporation) placement. Spasmolytic cocktail (5 mg verapamil) was given intraarterially through the radial sheath.

**Interventional procedures.** Standard guide catheters were used to perform PCI (standard shapes like Judkins, EBU, Amplatz) mostly 6 Fr. Standard guidewires for PCI, mostly Balance Middle Weight (Abbott Vascular) were used according to case specificity. Manual thrombus aspiration was performed in cases with high thrombus burden. Stent choice was performed with sealed envelope randomization.

**Anticoagulation and antiplatelet treatments.** Before PCI patients were treated with intravenous bolus of unfractionated heparin (100 IU/kg), aspirin (300 mg followed by 100 mg/day) and clopidogrel loading dose (600 mg followed by 75 mg/day for at least 1 year). After completion of PCI, weight-adjusted dosage protocol of heparin infusion was continued for 24 hours.

**Hemostasis management.** The radial artery sheath was removed immediately after the procedure and hemostasis was achieved by a simple bandage compression or TR band (Terumo Corporation). Simple bandage compression was applied with 4-6 small elastic bands, at the puncture site. The TR band was applied by inflating 13-15 ml of air and after each hour the TR band was gradually deflated and totally removed after 4 hours. Patient has no mobility restriction after the procedure.

**Study endpoints.** The primary endpoint of the study was target lesion failure (TLF) at 30 days, 1 and 2 years of follow up, defined as the composite of cardiovascular death, target vessel myocardial infarction (MI), or target vessel revascularization (TLR). The secondary endpoints were MI, TLR and definite stent thrombosis (ST) in both groups, comparing the survival rate between the patients in BVS and DES group.

**Definitions.** The criteria for TLF, MI and ST were consistent with the Academic Research Consortium (ARC). *Target lesion failure* was defined as the composite of cardiovascular death, target vessel myocardial infarction (MI), or target vessel revascularization (TLR). *Cardiovascular death* was defined as acute myocardial infarction, sudden cardiac death, death due to heart failure, death due to stroke, death due to cardiovascular procedures, death due to cardiovascular hemorrhage (intrapericardial bleed with cardiac tamponade) or death due to other cardiovascular causes after the index procedure. *Procedural success* was determined by angiographic success, defined as the achievement of a minimum stenosis diameter reduction to <20% in the presence of grade 3 TIMI flow. *Procedural time* was calculated as the time needed from the local anesthesia injection until guide catheter removal.

Control angiogram will be performed after 2 or 3 years from the index procedure to document the process of biodegradation of BVS with IVUS or OCT and measurements of minimal lumen diameter (MLD) of the vessel, minimal lumen area (MLA), minimal stent diameter (MSD) and minimal stent area (MSA).

**Statistical analysis.** Data were expressed as mean +/- standard deviation for normally distributed numeric variables, or reported as median (min/max) when the data did not fit a normal distribution. Percentages were used to express categorical variables. Categorical variables were compared with chi-square test or Fisher's exact test. Student's t-test or Mann Whitney U-test were used to compare differences between two groups (continuous data) when appropriate.

**Acute coronary syndrome.** ACS is caused by acute thrombosis induced by ruptured atherosclerotic plaque with or without vasoconstriction, resulting in sudden and critical reduction in blood flow.<sup>12</sup> Because of the fact that this situation can be life threatening condition, the criterias for risk stratification are so perform that clinician can made decisions for patient treatment and to individualized them to every different patient. Main symptom is chest pain, but classification is based on electrocardiographic changes. There are two category of patients:

- 1) Patients with acute chest pain and ST segment elevation >20 min (STE-ACS)
- 2) Patients with acute chest pain and non ST segment elevation (NSTE-ACS)

The incidencence of NSTE-ACS is higher and it is about 3 cases per 1000 population.<sup>13,14</sup> In hospital mortality is higher in STE-ACS (7%) comparing to NSTE-ACS (3-5%), but after 6 months mortality rate is almost the same (12% comparing to 13%).<sup>15,16</sup> Patients with NSTE-ACS are older, having more comorbidities, especially diabetes and renal failure. Epidemiology perception showed that treatment of NSTE-ACS should not be directed only to acute phase, but with the same intensity on long term period.<sup>17-23</sup>

There are several diagnostic criteria for ACS:

- Chest pain in rest lasting more than 20 minutes, "de novo" chest pain, or recent destabilization of exertional angina<sup>24-28</sup>
- electrocardiographic changes with ST segment depression > 1 mm (NSTEMI), transitory (less than 30 minutes) ST segment elevation > 1mm in at least two contiguous leads or ST segment elevation > 1mm in two standard leads or > 2mm in two conigues precordial leads (STEMI).<sup>29-31</sup>
- positive enzyme status – elevated cardiac markers in peiord for 24 hours, defined as elevated troponin T, troponin I, creatinin kinase (CK) and its cardiac isoenzyme (CK-MB) above the referent values.<sup>32-35</sup>
- coronary angiography, with coronary artery stenosis more than 70% or occlusion ("culprit lesion").

The recanalisation of culprit coronary artery is the basis of the ACS therapy. The first choise is mechanical recanalisation - percutaneous coronary intervention (PCI) through transradial approach (TRA)

because of the less bleeding comparing to transfemoral approach (TFA) and significant lower mortality and major cardiac events.<sup>36-39</sup>

**Bioresorbable vascular scaffold.** Bioresorbable vascular scaffold (BVS) – ABSORB (Abbott Vascular) is interventional percutaneous device for treatment of coronary artery disease. It is covered with bioresorbable polymer and cytostatic drug everolimus eluting in the coronary artery wall in the period of 1-2 months, preventing the uncontrolled neointimal hyperplasia. It is 4-th revolution in percutaneous coronary interventions after introducing balloon angioplasty in 1977, bare metal stents in 1988 and drug eluting stents in 2001 year.

After BVS implantation the process of its resorption is starting through natural metabolic process in the period of 2-3 years and after that period the BVS is fully resorbed from the coronary artery (**Figure 2**). The bioresorption of the scaffold stops the mechanical pressure on the coronary artery, allowing the return of the vasomotoric function and the lumen of the vessel itself. It is very important to mention the fact that there is no more structure which is mechanically caging the coronary vessel and normal vasomotoric response to physiologically stimulus is allowed, for example exercise or certain medications (**Figure 3**).

ABSORB Cohort A,<sup>40,41</sup> Cohort B,<sup>42</sup> i ABSORB EXTEND<sup>43</sup> clinical trials demonstrated excellent safety and efficacy.

- The great advantage of this vascular reparative therapy appear during the return of the vasomotoric function of the coronary vessel itself and the resorbable phase and are visible after the first year of its implantation. With these advantages BVS enables life acquisitions for the patients which were not possible up to now in interventional cardiology. The revascularisation is equal to best in class second generation DES treatment in the first three months, but with BVS drug releasing and vessel caging are temporary and are present during the healing of the coronary vessel.

- Expansion of the strategies for up to date treatment of the patients include widened use of invasive imaging techniques like intravascular ultrasound (IVUS), optical coherence tomography (OCT) and non invasive techniques like computerised tomography.<sup>43</sup>

- Extremely compatibility to the patients prone to allergic reactions with nickel and molybdenum which are releasing from the metallic stents and could be trigger mechanism for “in stent” restenosis.<sup>44,45</sup>

It is very important to be emphasised that first implantations of BVS were limited to patients with stable angina, one vessel coronary artery disease, lesions type A, lesions without calcification. Today their use is safe and spread even in very complicated cases with left main stenosis, patients with ACS including acute myocardial infarction with ST segment elevation and present thrombotic burden (**Figure 4**), tortuous coronary arteries, diabetic patients.

## Results

Until May 2015, 42 patients were enrolled in the study from the both groups.

**Group 1** – In this group 21 patients with ACS were enrolled with BVS implantation. Male patients were 66.7%, female 33.3% of the patients. In 14 patients (66.7%) BVS was implanted on left anterior descending artery (LAD), in 4 patients (19.0%) on right coronary artery (RCA) and in 3 patients (14.3%) on circumflex artery (Cx). Pre-procedural TIMI flow was 0 in 8 patients (38.1%), and TIMI 2-3 flow in 13 patients (61.9%). After the BVS implantation TIMI 3 flow was achieved in all 21 patients. Post-procedural diameter stenosis was 16.7 +/- 8.9%. No patients had angiographically visible residual thrombus at the end of

the procedure. OCT analysis was performed in 13 patients (61.9%) showed that the post-procedure mean lumen area was 7.88 +/- 1.84 mm<sup>2</sup>, minimum lumen area 5.52 +/- 1.59 mm<sup>2</sup>.

**Group 2** – In this control group 21 patients with ACS were enrolled with second generation DES implantation. Male patients were 71.4%, female 28.6% of the patients. In 13 patients (61.9%) DES was implanted on left anterior descending artery (LAD), in 6 patients (28.6%) on right coronary artery (RCA) and in 2 patients (9.5%) on circumflex artery (Cx). Pre-procedural TIMI flow was 0 in 9 patients (42.9%), and TIMI 2-3 flow in 12 patients (57.1%). After the DES implantation TIMI 3 flow was achieved in all 21 patients. Post-procedural diameter stenosis was 15.4 +/- 8.2. No patients had angiographically visible residual thrombus at the end of the procedure.

In all 42 patients, BVS and DES were successfully implanted without any complications, therefore device and procedural success were 100%. At the 30-day, 6-month (42 patients), 1 year (29 patients) and 2 years follow-up (16 patients) target-lesion failure rate was 0%. Non-target vessel revascularization, target vessel myocardial infarction (MI) or cerebrovascular insult were not reported. No episodes of cardiac death, scaffold or DES thrombosis were observed. All patients received dual antiplatelet therapy with Aspirin and Clopidogrel for 12 months.

### Discussion

The present study is single centre report for first BVS implantation in Republic of Macedonia, investigating the safety and clinical outcomes of BVS in patients with acute coronary syndrome.

Results of ABSORB Cohort A study report 5-year follow up at 29 patients with BVS implantation with major cardiovascular event (myocardial infarction without significant Q wave presence) at only one patient (3.4%). No episodes of cardiac death or scaffold thrombosis were observed.<sup>40,41</sup>

ABSORB Cohort B study report 2-year follow up at 100 patients with BVS implantation with major cardiovascular events in 9 patients (9.0%) (3 patients with non Q wave myocardial infarction and 6 patients with target lesion revascularisation). No episodes of cardiac death or scaffold thrombosis were observed.<sup>42</sup>

ABSORB EXTEND study report 6-month follow up at 269 patients with BVS implantation with major cardiovascular events in 7 patients (3.0%) (4 patients with non Q wave myocardial infarction and 3 patients with Q wave myocardial infarction). The incidence of target lesion revascularisation was very low (0.4%), scaffold thrombosis in 1 patient (0.4%) cardiac death in 1 patient (0.4%).<sup>43</sup>

All three studies revealed excellent safety and efficacy.

ABSORB II study which is the first randomized trial of the Absorb BVS (Abbott Vascular), enrolled 501 patients, 335 patients (with 364 lesions) received bioresorbable scaffold and 166 patients (182 lesions) received the metallic stent. The one year follow up indicates that the scaffold has similar clinical outcomes to an everolimus-eluting metallic stent (Xience, Abbott Vascular) at one year. There were no significant differences between groups in either the rate of the device-oriented clinical endpoint between groups (5% for the bioresorbable scaffold vs. 3% for the metallic stent; p=0.35), or the rate of the patient-oriented clinical endpoint (7% vs. 9% respectively; p=0.47). Also one year angina rates were significantly lower with bioresorbable scaffold compared with the metallic stent: 22% vs. 30%, respectively (p=0.04). Neither the overall rate of definite stent thrombosis (0.6% for the bioresorbable scaffold vs. 0% for the metallic stent; p=1) nor the overall rate of definite/probable stent thrombosis (0.9% vs. 0%, respectively; p=0.55) was significantly different between groups;

The US ABSORB III trial with 2250 patients enrolled will provide more data.<sup>46,47,48,49,50, 51</sup>

Recent studies have investigated the clinical outcome of BVS in the setting of the novo coronary artery lesions, mostly limited to type A lesions in patients presenting with stable angina. Theoretical advantages of BVS over metal stents include the fact that the bioresorption of the scaffold allows the recovery of physiological processes of endothelial vasomotor function, vascular remodelling and at a distance of time after implantation, lumen enlargement.<sup>52,53</sup>

It is important to emphasise that all interventions were performed through transradial approach, which lead to lower rate of bleeding events and consequently lower mortality rate.<sup>54, 55</sup>

The results in our study correlate with already published results from several relevant multicenter trials with bioresorbable scaffolds, especially with ABSORB II study. Our data apparently suggest that the outcome after the implantation of BVS is comparable to that of second generation drug-eluting stents. This study includes consecutive patients in a non-randomised design and further data are needed to provide a more definitive demonstration of safety and efficacy of this strategy. Despite this limitation, the present population is representative of "real-world" situations and our findings may therefore be more rapidly applicable to daily clinical practise.

### Conclusion

BVS implantation in patients presenting with ACS appeared feasible, it is safe and effective with high rate of final TIMI-flow III and good scaffold apposition and very low rate of major adverse cardiovascular events. Prudence and careful monitoring are essential in the adoption of a potentially revolutionary technique. Larger studies are currently needed to confirm these preliminary data. However, we cannot slowdown the progress of interventional cardiology while waiting for further megatrials.

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