

UNIVERSITY OF MEDICINE AND PHARMACY OF TÎRGU MUREŞ
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Abstract of the PhD thesis

**Impact of bioresorbable scaffolds utilization in the interventional
therapy of coronary atherosclerotic lesions**

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Myocardial revascularization presented a significant development over the past decades, leading to a significant change in clinical practice and therapeutic guidelines. The most commonly used therapeutic technique is percutaneous transluminal coronary angioplasty (PTCA) associated with implantation of coronary stents. Metallic and pharmacologically active stents are most commonly used in percutaneous interventions, but these devices present some disadvantages which may be overcome by the new developed devices, namely bioresorbable scaffolds (BVS).

Polymer-based BVS are designed not only to restore the vessel's patency, but also vascular motility following complete resorption of the stent material, thus removing the foreign material from the vascular wall. BVS are fourth generation stents, also representing the fourth revolution in interventional cardiology, being used in coronary revascularization in order to replace the first generation of metallic and pharmacologically active stents.

The implementation of coronary computed tomography angiography techniques and the improvement of the performance of those devices over time has led to the implementation of these technique in clinical practice. The role of CCTA was demonstrated not only in assessing the degree of coronary stenosis but also in evaluation of the arterial wall structure in which the atherosclerotic plaque develops. In addition, assessment of the global atherosclerotic coronary burden has been shown to play an important role in the follow-up of patients with atherosclerotic coronary artery disease, in terms of assessing the risk of major cardiac events, adjusting the treatment algorithm and applying primary and secondary prevention measures. Taking both the benefit of their radiolucency and their resorption over time, bioresorbable scaffolds offer high accuracy in the CCTA evaluation of treated lesions, thus opening up a new era in the follow-up methods of these devices.

The aim of this thesis was to evaluate the feasibility of CCTA assessment in evaluation of bioresorbable coronary scaffolds and the use of this technique in the follow-up of these devices. Secondly, the progression of atherosclerotic plaques was evaluated after BVS implantation, as well as procedural aspects related to preparation, implantation and optimization techniques of these devices. Moreover, shear stress improvement after BVS implantation was studied.

This is a prospective observational study which enrolled 67 patients between January 2015 and March 2017, admitted in Cardio Med Medical Center Tirgu-Mures, elective treated for the diagnosis of stable/unstable angina pectoris via implantation of one or more bioresorbable scaffolds on the basis of European Society of Cardiology guidelines indications for revascularization. Overall, 103 devices were implanted. In order to compare the BVS with metallic stents a control group of 43 patients with same inclusion and exclusion criteria as well as the same evaluation and follow-up methodology were included, with 63 metallic stents implanted. Each patient was angiographically non-invasively evaluated via CCTA at 12-24 months after PTCA.

The aim of **Substudy 1** was to evaluate the utility of CCTA assessment in the follow-up of bioresorbable versus metallic stents for the diagnosis of in-stent restenosis after PTCA. We conducted a prospective observational study on 73 patients. On the basis of stent type, subjects of the study were divided in two groups as follows: Group 1 - included 30 patients with 50 implanted BVS, Group 2 - which included 43 patients with 63 metallic implanted stents. The comparative analysis of Angio-CT sensitivity in the visual evaluation of in-stent restenosis diagnosis, in the two groups, demonstrated a significantly higher percentage of diagnostic CCTA in the group of bioresorbable stents (94% group 1 vs. 76.19% group 2, $p = 0.0006$). Therefore, CCTA evaluation of BVS is superior to metallic stents evaluation, the latter being influenced by numerous sources of error, mainly dependent on the presence of the metallic structure.

Substudy 2 was an CCTA-based study of the atherosclerotic plaque progression after BVS implantation. This was an observational, prospective study conducted on 30 patients, in order to evaluate the impact of BVS implantation and the influence of pre- and post-implantation preparing techniques on the structure and morphology of the coronary artery. 80% of the lesions were predilated. Significant changes were noted in both the morphology of coronary plaques treated with these devices and in the lumen and coronary wall after BVS implantation. Regarding CT vulnerability markers, the study groups presented significant differences in terms of positive remodeling (37.5% in subgroup with pre-dilatation lesions vs. 60% in subgroup without pre-dilatation lesions, $p = 0.001$) In terms of vascular volume ($324.8 \pm 60.58 \text{ mm}^3$ - post-dilatation lesions vs. $217.0 \pm 103.8 \text{ mm}^3$ - lesions without post-dilatation, $p = 0.009$) and volume lumen ($158.8 \pm 34.71 \text{ mm}^3$ - post-dilatation lesions vs. $106.4 \pm 49.98 \text{ mm}^3$ - without post-dilatation, $p = 0.001$) the study groups presented significant differences. The lipid volume and lipid % ($20.07 \pm 15.67 \text{ mm}^3$ and $10.31 \pm 6.24\%$ in subgroup pre-implantation lesions vs. $11.05 \pm 10.83 \text{ mm}^3$ and $6.46 \pm 6.14\%$ in subgroup post-implantation lesions, $p = 0.01$) presented a significant reduction after BVS implantation. The CT assessment of atherosclerotic plaques and BVS is a new non-invasive follow-up technique of these devices which can be introduced as a reference method. Proper preparation of the lesions, both as accurate choosing and implanting process of the bioresorbable scaffolds was crucial in order to achieve a good outcome and to reduce the risk of subsequent coronary events.

Substudy 3 - Shear Stress improvement after BVS implantation. This study aims to evaluate the shear stress at the level of coronary lesions, respectively in the implanted BVS. At the same time, the differences between shear stress values at different points of the coronary artery, respectively in the implanted BVS, as well as the correlation between shear stress and the necrotic core, were evaluated via non-invasive technique. This was an observational, prospective study conducted on 30 patients. Angio-CT evaluation was performed before and after BVS implantation for 15 of the patients, and only after BVS implantation for the other 15 subjects of the study, with 69 coronary plaques analyzed, 48 of which were treated with bioresorbable scaffolds.

This study demonstrates a statistically significant correlations between mean shear stress values before maximum stenosis, in an assessment before and post-implantation of BVS (pre-BVS $3.39 \pm 1.93 \text{ Pa}$, post-BVS $1.91 \pm 0.68 \text{ Pa}$, $p < 0.0001$). Pre-interventional value of mean shear stress was increased, normalizing after BVS implantation (pre-BVS $3.39 \pm 1.93 \text{ Pa}$, post-BVS $1.91 \pm 0.68 \text{ Pa}$, $p < 0.0001$), thus demonstrating the benefit of bioresorbable scaffolds in atherosclerotic coronary lesions. Moreover, a statistically significant correlation was obtained between mean shear stress, pre- and post-implantation of BVS (pre-BVS $2.87 \pm 1.64 \text{ Pa}$, post-BVS 1.9 ± 0.49 , $p = 0.0001$), as well as for the maximum shear stress pre- and post-implantation of BVS (pre-BVS $11.78 \pm 10.06 \text{ Pa}$, post-BVS $6.35 \pm 3.08 \text{ Pa}$, $p = 0.0009$), thus uniformizing intra-coronary blood flow, as a protective factor for the development and progression of new atherosclerotic plaques.

This thesis has scientifically demonstrated the usefulness of BVS in the treatment of atherosclerotic coronary lesions and the feasibility of their follow-up assessment via non-invasive techniques.