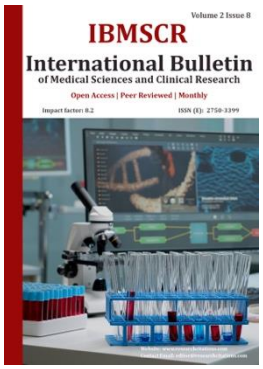

MID-TERM AND LONG-TERM OUTCOMES OF USING MAGMARIS BVS STENTS IN PATIENTS WITH ACUTE CORONARY EVENTS

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Objective: To investigate the mid-term and long-term outcomes of using the next-generation Magmaris BVS stents in patients with acute coronary syndrome (ACS).

Materials and Methods: A total of 64 patients with acute coronary syndrome were examined, including 49 males and 15 females. The mean age of the participants was 54.3 ± 9.2 years (ranging from 33 to 79 years). Acute coronary syndrome comprised two nosological units: non-ST-elevation myocardial infarction (NSTEMI) in 33 patients (Group 1) and ST-elevation myocardial infarction (STEMI) in 31 patients (Group 2). All patients received the biodegradable Magmaris stent. Statistical significance was considered at $p < 0.05$.

Results: In 9.1% of cases, the implantation of the Magmaris stent in patients with NSTEMI was associated with the development of intrastent thrombosis, which was likely attributed to decreased adherence to medication therapy, particularly dual antiplatelet therapy ($p > 0.05$). High adherence to medication therapy, especially dual antiplatelet therapy, among patients with the more severe form of the disease (STEMI), ensured good mid-term and long-term outcomes of using Magmaris BVS stents.

Conclusion: We hope that our study will contribute to the development and improvement of new technologies in modern bioengineering. Through the integration of these developments into various medical fields, future devices should lead to the creation of optimized designs with high levels of safety and efficacy, facilitating their broader implementation in clinical practice.

Keywords: *biodegradable stent, ischemic heart disease, acute myocardial infarction, coronary angiography.*

Introduction.

BVS scaffolds marked the fourth revolution in interventional cardiology. Ultimately, their development aimed to overcome the limitations of drug-eluting stents (DES) by providing temporary support to the vessel wall while allowing the release of an anti-proliferative drug to limit excessive response, potentially enabling vessel healing and restoration of its physiological functions.

Magmaris is a Class III medical device according to Directive 93/42/EEC. It is made of a magnesium alloy and equipped with permanent tantalum radiopaque markers of rounded shape located at both ends of the device. The scaffold itself is radiolucent, with only the stent markers visible under fluoroscopy. The stent scaffold is coated with a polymer coating containing a drug substance. The nominal content of the drug substance in each scaffold is 1.4 µg of sirolimus per 1 mm^2 of scaffold surface area. Magmaris received CE-mark conformity on June 15, 2016. Conclusions regarding the safety and efficacy of Magmaris, and therefore its compliance with essential requirements, are based on clinical results from BIOSOLVE-II, -III, and -IV studies. Preliminary study data demonstrated that the frequency of early and late complications when using Magmaris was very low, indicating a very good safety profile, and the frequency of complications related to target lesion failure (TLF) and scaffold thrombosis (TSc) was comparable to various second-generation DES.

The use of BVS scaffolds in our Republic is currently limited. However, studying their use with an assessment of near-term, mid-term, and long-term results is highly relevant.

Objective. To investigate the mid-term and long-term outcomes of using the next-generation Magmaris BVS scaffold in patients with acute coronary syndrome (ACS)

Materials and methods

A total of 64 patients with acute coronary syndrome (ACS) were evaluated, including 49 males and 15 females. The mean age of the patients was 54.3±9.2 years (ranging from 33 to 79 years). ACS comprised two nosological entities: non-ST-elevation myocardial infarction (NSTEMI) in 33 patients and ST-elevation myocardial infarction (STEMI) in 31 patients.

Within the first 24-48 hours of hospitalization, patients underwent comprehensive assessments, including physical examination, 12-lead electrocardiography (ECG), echocardiography (Echo), clinical and biochemical blood tests (including tests for syphilis, HIV, and hepatitis), and coagulation studies. Additionally, coronary angiography (CAG) was performed within the first 24 hours of hospitalization for all patients, assessing the TIMI scale and stenosis according to the ACC/AHA classification (2007). Endovascular treatment via percutaneous coronary intervention (PCI) was performed for all 64 patients, with the implantation of the Magmaris biodegradable scaffold.

Upon discharge, all patients were prescribed standard medical therapy, including dual antiplatelet therapy (DAPT), beta-blockers, statins, proton pump inhibitors (PPIs), and, if necessary, angiotensin-converting enzyme inhibitors (ACEIs) or angiotensin II receptor antagonists (ARBs); for patients with type 2 diabetes mellitus, hypoglycemic agents were also administered.

Follow-up assessments were conducted at 6 and 12 months post-PCI with scaffold implantation to evaluate the efficacy of PCI with Magmaris scaffold implantation in terms of major adverse cardiac events (MACE), which encompassed scaffold thrombosis (ST), target

vessel revascularization (TVR), target vessel myocardial infarction (TV-MI), and cardiac death (CD).

Patients were stratified into two groups based on their diagnosis: Group 1 comprised 33 patients with NSTEMI, and Group 2 comprised 31 patients with STEMI.

Statistical analysis was performed using the Statistica 6.0 software package on a Pentium-IV personal computer. Descriptive statistics included mean and standard deviation (SD). Differences between qualitative variables were assessed using the chi-square (χ^2) test, while continuous variables with normal distribution were compared using Student's t-test. Correlation analysis was conducted using Pearson's correlation coefficient. Differences were considered statistically significant at $p<0.05$. Data are presented as mean ± SD.

Results.

A comparative analysis of the nature of pharmacological therapy at the time of discharge from the hospital did not reveal significant differences between the compared groups (Table 1). All patients, both with NSTEMI and STEMI, were prescribed dual antiplatelet therapy (DAPT), statins, beta-blockers, and proton pump inhibitors (PPIs). Only nitrates, calcium antagonists (CA), and diuretics (including potassium-sparing diuretics) were prescribed more frequently in Group 2 patients compared to Group 1 patients, which was attributed to the more severe clinical status of these patients. However, the observed differences did not reach statistical significance (all $p>0.05$).

Table 1.

Medication therapy in the compared patient groups at the time of discharge from the hospital

Medication group	**1 group (NSTEMI) n =33**	**Group 2 (STEMI) n =31**
DAAT	33 (100%)	31 (100%)
Statins	33 (100%)	31 (100%)
BAB	33 (100%)	31 (100%)
IPP	33 (100%)	31 (100%)
Nitrates	4 (12.1%)	7 (22.6%)
ACEI	15 (45.4%)	13 (41.9%)
ARA-2	11 (33.4%)	10 (32.3%)
AK	7 (21.2%)	8 (25.8%)
Diuretics	2 (6.1%)	4 (12.9%)
K^+	14 (42.4%)	16 (51.6%)
Hypoglycemic	8 (24.2%)	8 (25.8%)

Notes: DAPT - Dual antiplatelet therapy; BAB - Beta-blockers; ACEI - Angiotensin-converting enzyme inhibitors; ARA-2 - angiotensin-2 receptor antagonists; AK - Calcium antagonists; K^+ - potassium-sparing diuretics; PPI – proton pump inhibitors; all p>0.05.

The assessment of changes in medication adherence among patients with NSTEMI (Group 1) over six months revealed a decrease in adherence to therapy. Specifically, the intake of DAPT and ACE inhibitors decreased by 12.1%; statins by 15.2%; beta-blockers and calcium

antagonists by 6.1%; PPIs by 18.2%; ARBs by 3.1%; and potassium-sparing diuretics by half. However, the intake of hypoglycemic agents remained unchanged, likely due to the influence of the underlying pathology - type 2 diabetes mellitus (Table 2).

Evaluation of therapy adherence one year post-PCI among Group 1 individuals showed that DAPT intake increased by 9.0% compared to the six-month stage but was 3.1% lower than the initial levels. Thus, adherence to DAPT decreased in the first six months, leading to the development of TS, which, in turn, contributed to increased therapy adherence, but not in all patients.

A similar pattern of decrease and subsequent increase in therapy adherence was observed for PPIs: adherence decreased by 12.1% at the six-month stage and increased by 6.1% at the twelve-month stage compared to the six-month stage but did not reach the initial levels.

At the twelve-month stage, a decrease in the intake of the following medication groups was observed (Table 2):

- Statins by 21.2% compared to the initial stage and by 6.0% compared to the six-month stage ($p<0.05$);
- Beta-blockers by 15.2% and 9.1%;
- ACE inhibitors by 15.1% and 3.0%;
- ARBs by 3.1% and 3.1%;
- Calcium antagonists by 6.1% and 6.1%;
- Potassium-sparing diuretics by 30.3% and 9.1%, respectively.

Due to improved clinical status, the intake of nitrates and diuretics was no longer required at the six-month stage. However, hypoglycemic agents remained on lifelong therapy (as diabetes is currently an incurable disease), as observed in our patients (Table 2).

Table 2.

Dynamics of drug therapy among patients with NSTEMI

Medication group	**Outcome n =33**	**6 months n =33**	**p1**	**12 months n =33**	**p2**
			χ2		**χ2**
DAAT	33 (100%)	29 (87.9%)	0.122	32 (96.9%)	1,000
			2,395		0.000
Statins	33 (100%)	28 (84.8%)	0.063*	26 (78.8%)	**0.016**
			3,462		**5,753**
BAB	33 (100%)	31 (93.9%)	0.473	28 (84.8%)	0.063*
			0.516		3,462
IPP	33 (100%)	27 (81.8%)	0.032	29 (87.9%)	0.122
			4,583		2,395
Nitrates	4 (12.1%)	-	0.122	-	0.122
			2,395		2,395
ACEI	15 (45.4%)	11 (33.3%)	0.450	10 (30.3%)	0.310
			0.571		1,030

ARA-2	11 (33.4%)	10 (30.3%)	1,000 0.000	10 (30.3%)	1,000 0.000
AK	7 (21.2%)	5 (15.1%)	0.750 0.102	5 (15.1%)	0.750 0.102
Diuretics	2 (6.1%)	-	0.473 0.516	-	0.473 0.516
K $^{+}$	14 (42.4%)	7 (21.2%)	0.113 2,514	4 (12.1%)	**0.013** **6,188**
Hypoglycemic	8 (24.2%)	8 (24.2%)	0.774 0.083	8 (24.2%)	0.774 0.083

*Notes: DAPT - Dual antiplatelet therapy; BAB - Beta-blockers; ACEI - Angiotensin-converting enzyme inhibitors; ARA-2 - angiotensin-2 receptor antagonists; AK - Calcium antagonists; K $^{+}$ - potassium-sparing diuretics; PPI – proton pump inhibitors; * - tendency towards reliability; p1 - reliability of differences between the outcome data and the 6-month stage; p2 – significance of differences between the outcome data and the 12-month stage*

Adherence to medication therapy at different stages was found to be more positive among patients in Group 2 (i.e., diagnosed with STEMI) compared to similar indicators in patients in Group 1 (i.e., diagnosed with NSTEMI) (Table 3).

Table 3.

Dynamics of drug therapy use among patients with STEMI

Medication group	**Outcome n =31**	**6 months n =31**	**12 months n =30**
DAAT	31 (100%)	31 (100%)	30 (100%)
Statins	31 (100%)	30 (96.8%)	30 (100%)
BAB	31 (100%)	30 (96.8%)	28 (93.3%)
IPP	31 (100%)	29 (93.5%)	28 (93.3%)
Nitrates	7 (22.6%)	-	-
ACEI	13 (41.9%)	12 (38.7%)	10 (33.3%)
ARA-2	10 (32.3%)	10 (32.3%)	9 (30.0%)
AK	8 (25.8%)	6 (19.3%)	5 (16.7%)
Diuretics	4 (12.9%)	3 (9.7%)	1 (3.3%)
K $^{+}$	16 (51.6%)	15 (48.4%)	10 (33.3%)
Hypoglycemic	8 (25.8%)	8 (25.8%)	8 (26.7%)

Notes: DAPT - Dual antiplatelet therapy; BAB - Beta-blockers; ACEI - Angiotensin-converting enzyme inhibitors; ARA-2 - angiotensin-2 receptor antagonists; AK - Calcium antagonists; K $^{+}$ - potassium-sparing diuretics; PPI – proton pump inhibitors; all p>0.05

Adherence to medication therapy at different stages was found to be more positive among patients in Group 2 (i.e., diagnosed with STEMI) compared to similar indicators in patients in Group 1 (i.e., diagnosed with NSTEMI) (Table 3).

In particular, throughout the study, all patients continued to take DAPT, and the intake of statins, beta-blockers, and PPIs remained above 90% (Table 3).

At the end of the 12-month study period, 30 patients from Group 2 were included, while one patient did not attend the 12-month follow-up (they had left the country) and was excluded from the analysis.

Table 3 provides detailed dynamics of the medication groups taken by patients with STEMI. As shown in Table 3, all (100%) patients in Group 2 continued to take DAPT until the end of the study.

A decrease in adherence was observed for the following medication groups (Table 3):

- Statins – by 3.2% at the 6-month stage compared to baseline, but adherence returned to 100% at the 12-month stage;
- Beta-blockers – by 3.2% and 6.7% at the 6 and 12-month stages post-PCI, respectively;
- PPIs – by 6.5% at both the 6 and 12-month stages;
- ACE inhibitors – by 3.2% and 8.6%;
- ARBs – by 0% and 2.3%;
- Calcium antagonists – by 6.5% and 9.1%;
- Diuretics – by 3.2% and 9.6%;
- Potassium-sparing diuretics – by 3.2% and 18.3%, respectively.

Similar to Group 1, adherence to hypoglycemic agents remained unchanged and consistent (Table 3).

The decrease in medication therapy adherence at the 6-month stage led to a cumulative MACE rate of 9.1% among patients in Group 1, which included three cases of scaffold thrombosis (ST). Specifically, two patients independently stopped taking DAPT, and three months later, scaffold thrombosis developed in them. Another patient also discontinued DAPT, and four months after PCI, scaffold thrombosis occurred.

Possibly, the less severe form of the disease (NSTEMI) and awareness of the subsequent scaffold resorption contributed to the early voluntary discontinuation of medication therapy, particularly DAPT, which ultimately resulted in a 9.1% MACE rate among patients in Group 1 or a 4.7% MACE rate overall in the study population with the implantation of the next-generation biodegradable scaffolds Magmaris.

A similar evaluation of adherence levels in relation to the development of MACE showed that high sustained adherence to therapy, particularly to DAPT, among patients with STEMI likely contributed to the absence of MACE at all subsequent stages (Table 4). This could be interpreted as a good effectiveness of the Magmaris scaffold in terms of application in patients with acute coronary syndrome, particularly with STEMI.

Table 4.

Dynamics of MACE in the compared groups of patients

MACE		**1 group (NSTEMI)**	**Group 2 (STEMI)**
Stages:		**n =33**	**n =31**
6 months:	TS with	3 (9.1%)	0

	TVR	0	0
	TV - MI	0	0
	CD	0	0
12 months:	T.S.	3 (9.1%)	0
	TVR	0	0
	TV - MI	0	0
	CD	0	0
TOTAL (n=64)		3 (4.7%)	
TS – stent thrombosis of stent); TVR – target vessel revascularization (target vessel revascularization); TV - MI – heart attack myocardium target vessel (target vessel myocardial infarction); CD – cardiac death.			

During the correlation analysis between the nosological component and the cumulative MACE rate, an inverse relationship was established, although it did not reach statistical significance (Figure 1). In other words, a less severe form of the disease, particularly NSTEMI, was associated with a more frequent occurrence of adverse cardiac events (MACE), specifically scaffold thrombosis (ST).

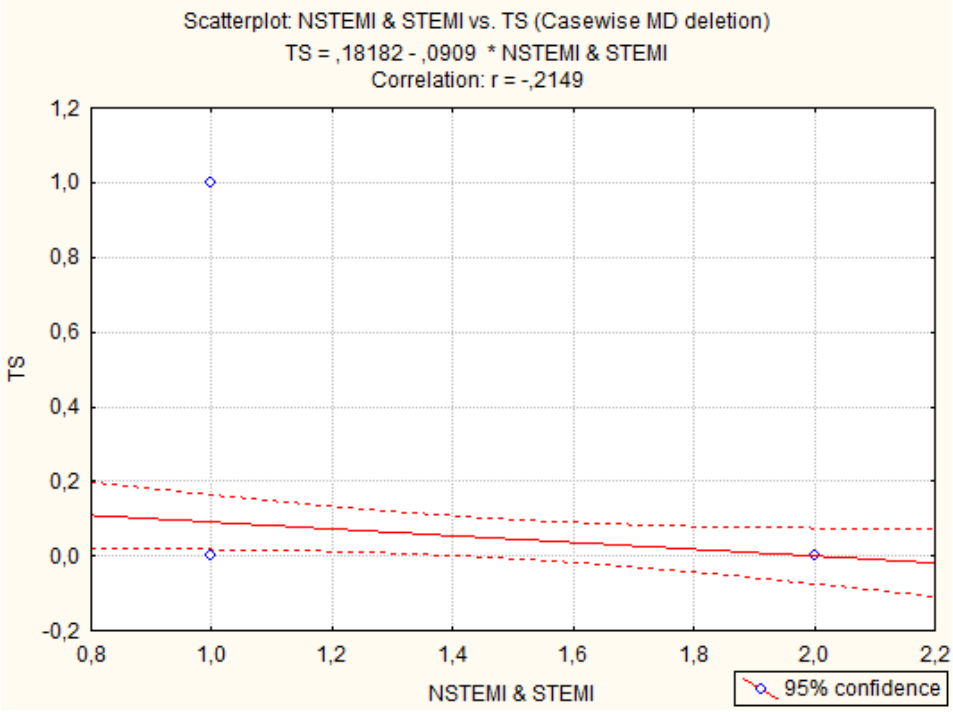

Figure 4.1. **Correlation plot between nosological components and cases of scaffold thrombosis (ST). p=0.088; r= -0.214 and t= -1.732**

Notes: On the X-axis, labeled "1," patients diagnosed with NSTEMI are indicated, and labeled "2," patients diagnosed with STEMI; on the Y-axis - cases of scaffold thrombosis.

Discussion.

The use of BVS scaffolds in patients with coronary artery disease (CAD) is currently limited in routine clinical practice due to safety concerns and the 2018 European Society of Cardiology recommendations on myocardial revascularization, which do not recommend the use of BVS scaffolds for clinical use outside of clinical trials [4]. However, there is increasing positive data

on the efficacy and safety of using BVS scaffolds in patients with stable CAD and in certain patients with acute coronary syndromes (ACS).

To date, the concept of BVS scaffolds remains attractive. One promising representative of this type of device is the Magmaris scaffold — a new scaffold made of a bioresorbable magnesium alloy, fully coated with a biodegradable polymer poly-L-lactic acid (PLLA) "BIOlute". Initial data have shown an acceptable safety profile for this device, especially in terms of scaffold thrombosis.

In the PRODIGY study, 2013 patients were randomized to receive DAPT (aspirin + clopidogrel) for 6 and 24 months with a primary composite outcome of all-cause mortality, MI, stroke, or major bleeding. Analysis of net MACE demonstrated an increase in their incidence when extending DAPT in the stable CAD group (13.3 vs. 5.6%; OR 2.5; 95% CI [1.35–4.69]; p=0.004), but not in patients with ACS (16.1 vs. 14.1%; OR 1.15; 95% CI [0.88–1.50]; p=0.29) [5].

Several other studies conducted since 2014 have confirmed the superiority of short-course DAPT, the largest of which was the ISAR-SAFE study - a double-blind randomized study that included 4005 patients, 60% of whom had stable CAD and 40% had ACS. The study compared 6-month DAPT (aspirin + clopidogrel) with 12-month DAPT and found no differences in the frequency of the primary composite endpoint in both ACS and stable CAD patients [6].

In the study by Michael J. Lipinski et al. [7], it was found that in 5 out of 14 cases, BVS scaffold thrombosis occurred after discontinuation of DAPT, leading the authors to recommend avoiding the use of BVS scaffolds in individuals requiring PCI if there are concerns about non-adherence to the treatment regimen.

Our work indicates that the Magmaris BVS scaffold can be used in patients with acute coronary syndromes, but strict control over DAPT adherence is necessary

Conclusion.

Installation of the Magmaris bioresorbing frame in patients with NSTEMI in 9.1% of cases was accompanied by the development of intraframe thrombosis, which was probably due to a decrease in adherence to drug therapy, especially to DAPT therapy (p>0.05)

High adherence to drug therapy, and in particular to DAAT tolerance, among patients with a more severe form of the disease (STEMI) ensured good mid-term and long-term results using Magmaris BVS frames.

We hope our work will contribute to developing and improving new technologies of modern “bioengineering”. By integrating these developments into various areas of the medical industry, future devices should lead to optimized designs with high safety and effectiveness, ensuring their wider implementation in clinical practice.

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