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Long-term outcomes of patients treated with sirolimus-eluting resorbable magnesium scaffolds: Insights from the SHERPA-MAGIC study

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ABSTRACT

Background: The resorbable magnesium scaffold (RMS) is a second-generation bioresorbable scaffold (BRS) that has shown conflicting results in previous studies. These findings suggest that patient selection and implantation technique may have an impact on clinical outcomes. This study aimed to investigate the safety and long-term effectiveness of RMS in a narrowly selected population.

Methods: SHERPA-MAGIC is an investigator-driven, multicenter, prospective, single-arm study that enrolled patients undergoing BRS coronary implantation in 18 Italian centers. The present analysis considered the first 543 enrolled patients treated with RMS, with a minimum follow-up of 1 year. The study protocol included strict criteria for patient selection and standardization of RMS implantation. The primary outcome was the occurrence of the vessel-oriented composite endpoints (VOCE), including cardiac death, target vessel myocardial infarction, and ischemia-driven target vessel revascularization.

Results: Overall, 635 vessels were treated. The 1-year cumulative occurrence of VOCE was 22 (3.5%, 95% CI 2.2%–5.2%), which was significantly lower than the prespecified estimation (from 5.5% to 8.5%). At the median follow-up of 3.5 [2.6–4.3] years, there were 3 (0.5%) cardiac deaths, 12 (1.9%) target vessel myocardial infarctions, and 33 (5.2%) ischemia-driven target vessel revascularizations. A total of 37 (5.8%, 95%CI 4.1%–7.9%) VOCEs were detected. Scaffold thrombosis occurred in 4 (0.6%, 95%CI 0.1%–1.6%) cases. Patient-level analysis confirmed the findings of the vessel-level analysis.

Conclusions: These results confirm the safety and performance of RMS technology. If confirmed in randomized controlled trials, they may rekindle interest in the use of scaffolds in daily practice.

Abbreviations and acronyms: BRS, Bioresorbable scaffolds; DES, Drug-eluting stent; RMS, Resorbable magnesium scaffold; PCI, Percutaneous coronary intervention; VOCE, Vessel-oriented composite endpoints; POCE, Patient-oriented composite endpoints.

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1. Introduction

Bioresorbable scaffolds (BRS) have been developed to overcome the limitations of second-generation drug-eluting stents (DES) relating to permanent intracoronary metallic structures. The latter are responsible for an inflammatory status of the coronary wall, leading to an incidence rate of about 2%/year of very late cardiac events [1]. When comparing DES and the first generation of BRS (Absorb, Abbott Vascular, Santa Clara, CA), the latter showed a significant increase in adverse events [2]. Resorbable magnesium scaffold (RMS, Magmaris, Biotronik AG, Buelach, Switzerland) is a second-generation BRS. Initial studies have yielded inconsistent results, indicating that the selection of patients and the method of implantation may have a crucial role in the determination of the long-term outcome [3–7]. Consequently, additional data and further studies with long-term outcomes are necessary to evaluate the safety and efficacy of RMS and determine if the potential benefits of a resorbable technology can be applied in clinical practice.

The objective of this study is to document the long-term clinical outcomes of the initial 543 patients treated with RMS in the Scaffold Implantation in Emilia-Romagna Plus Multi Absorbable Gears Intra Coronary (SHERPA-MAGIC) study.

2. Materials and methods

2.1. Study design

The SHERPA-MAGIC is an investigator-driven, multicenter, prospective, single-arm study that enrolls consecutive patients undergoing percutaneous coronary intervention (PCI) with implantation of BRS in 18 Italian centers. A summary of the design has been previously reported [8]. The first patient of the SHERPA-MAGIC study was enrolled in December 2017, and both enrollment and follow-up are still ongoing. The present analysis considered the first 543 enrolled patients treated with RMS in at least one coronary artery and had a minimum follow-up of 1 year. The study was conducted in accordance with the ethical principles of the Declaration of Helsinki. Patients were informed that their participation was voluntary and provided written informed consent. The study was registered (www.clinicaltrials.gov with identifier NCT03327961) and received ethical approval from the institutional review boards of the participating hospitals.

2.2. Protocol criteria for eligible patients and recommendations for RMS implantation

The decision to proceed with PCI was made in accordance with current guidelines and/or institutional protocols and was performed using standard materials and techniques. The decision to implant RMS was at the discretion of the operator and was in accordance with the patient selection criteria outlined in the SHERPA-MAGIC protocol. The shared criteria that qualified a patient as ideal for RMS implantation were: i) first event, and/or ii) opportunity to achieve complete revascularization in patients under 65 years of age, and/or iii) revascularization of long lesions (>24 mm), particularly those located in the left anterior descending (LAD) coronary artery, and/or iv) spontaneous coronary dissection. Furthermore, the target lesion had to meet the following criteria: i) reference vessel diameter between 2.8 and 3.8 mm, ii) lack of severe coronary calcifications, non-ostial location, and a low probability of requiring bifurcation stenting. Patients who had a clinical indication for oral anticoagulant therapy were not eligible for the study. The SHERPA-MAGIC protocol also standardized the steps of RMS implantation, which included: i) mandatory predilatation, ii) sizing 1:1, iii) mandatory post-dilation with non-compliant balloon (up to 0.5 mm larger than the scaffold diameter). The use of intravascular ultrasonography (IVUS) or optical coherence tomography (OCT) was strongly encouraged. Standard pharmacotherapy was administered in accordance with the current guidelines, and dual antiplatelet therapy (DAPT) was prescribed for at least 12 months [9]. Clinical follow-up occurred at 1, 6, and 12 months and annually thereafter.

2.3. Data collection

All clinical, lesion, and outcome data were prospectively collected using a dedicated electronic case report form (eCRF). The academic research organization (University of Ferrara, Ferrara, Italy) of the coordinating centre periodically conducted monitoring and verification of the data. Angiograms were prospectively collected, and quantitative coronary analysis (QCA) was performed at an independent core laboratory (University of Ferrara, Ferrara, Italy) without knowledge of the patient's outcomes. Angiographic analyses were conducted for all target vessels using an automated edge-detection algorithm (QAngio XA 7.3, Medis Medical Imaging Systems, Leiden, Netherlands).

2.4. Outcomes

The main analysis was carried out at vessel-level. The primary study endpoint was the vessel-oriented composite endpoints (VOCE), defined as the composite of cardiac death, target vessel myocardial infarction (TVMI) and ischemia-driven target vessel revascularization (id-TVR). The target vessel(s) referred to the vessel(s) treated with RMS. Secondary endpoints included the individual components of the primary endpoint. The safety endpoint was the incidence of scaffold thrombosis. The prespecified time-point of the primary endpoint was at 1-year. However, due to the limited number of patients and adverse events, the present analysis reports data outcome at the longest available follow-up (November 2022). Adverse events were adjudicated by a clinical events committee, who reviewed original source documents. In case of repeated adverse events, the first that occurred was the one considered. The committee classified event as target-vessel related or not based on the available information (i.e., electrocardiogram, cardiac biomarkers, echocardiography, coronary artery angiography). In the case of cardiovascular death in patients with multiple study vessels, the event was attributed to each vessel [10]. Scaffold thrombosis was classified in agreement with the Academic Research Consortium consensus document [11].

2.5. Ancillary analyses: patient-oriented composite endpoints and propensity matching

To assess the robustness of the findings, adverse events were also reported at patient-level (patient-oriented composite endpoints, POCE, defined as the composite of all-cause death, MI and ischemia-driven coronary revascularization). Given the previous concerns about the safety of RMS in MI patients, a propensity score matched analysis was conducted comparing MI patients of the SHERPA-MAGIC study with a matched cohort of MI patients from the Acute coRonary sYndrOmes proSpective regisTry Of Ferrara (ARYOSTO) study (NCT02438085). The ARYOSTO study is a prospective, single-center study that collects data on baseline characteristics, treatment, and outcomes of all patients admitted to the University Hospital of Ferrara with a diagnosis of acute coronary syndrome [12]. The ARYOSTO study began in May 2015 and is ongoing. For the present purpose, we included patients admitted to the hospital from January 2018 to December 2021 and treated with second-generation DES ($n = 2725$). The endpoint for the comparison between SHERPA-MAGIC and ARYOSTO matched cohorts was POCE.

2.6. Statistical analysis

The sample size calculation of the SHERPA-MAGIC study was based on an estimated 1-year VOCE around 7% [3–7]. Estimating a tolerance margin of around 1.5%, at least 1111 patients were required. Due to the progressive slowdown in enrolment (2017: 10 patients, 2018: 211 patients, 2019: 172 patients, 2020: 108 patients, 2021: 42 patients), the

Table 1
Study patients and vessels.

	Total
	Patients ($n = 543$)
Age, (years)	56 ± 9
Male sex, no. (%)	433 (78)
CV risk factors, no. (%)	
Diabetes	81 (15)
Hypertension	291 (54)
Hyperlipidemia	287 (53)
Current smoker	216 (40)
Former smoker	125 (23)
Medical history, no. (%)	
MI and/or PCI	67 (12)
COPD	10 (2)
PAD	24 (4)
Clinical presentation	
STEMI, no. (%)	163 (30)
NSTEMI, no. (%)	239 (44)
CCS, no. (%)	141 (26)
Other data	
BMI, Kg/m^2	27 [24–29]
Creatinine clearance, mg/ml	115 [90–140]
LVEF (%)	58 [50–60]
Medical therapy, no. (%)	
Aspirin	543 (100)
Ticagrelor	388 (72)
Prasugrel	57 (10)
Clopidogrel	98 (18)
ACE inhibitor/A2R blocker	323 (60)
High-potency statin	520 (96)
Ezetimibe	288 (53)
PCSK9 inhibitor	25 (5)
	Vessels ($n = 635$)
Target vessel, no. (%)	
Left anterior descending	363 (57)
Left circumflex	111 (18)
Right coronary	161 (25)
Lesion characteristics, no. (%)	
-de novo	628 (99)
-spontaneous coronary dissection	7 (1)
AHA/ACC classification, no. (%)	
-A	35 (5)
-B1	141 (22)
-B2	182 (29)
-C	277 (44)
Bifurcation	95 (15)
Severe calcification	10 (2)
Severe tortuosity	11 (2)
Quantitative coronary analysis	
Reference vessel diameter, mm	2.7 [2.4–3]
Minimal lumen diameter, mm	0.9 [0.6–1.2]
Diameter stenosis, %	69 [55–80]
Lesion length, mm	21 [15–29]
Procedural details, no. (%)	
Predilatation, no. (%)	606 (95)
Largest pre-dilation balloon, mm	2.5 [2.5–3]
RMS diameter, mm	3.5 [3–3.5]
Total RMS length, mm	25 [20–35]
Overlapping RMS, no. (%)	194 (31)
Post-dilatation, no. (%)	632 (99)
Largest post-dilation balloon, mm	3.5 [3.5–3.75]
Intracoronary imaging, no. (%)	355 (56)
-IVUS	279 (44)
-OCT	76 (12)

CV: cardiovascular. MI: myocardial infarction. COPD: chronic obstructive pulmonary disease. PAD: peripheral artery disease. STEMI: ST-segment elevation MI. NSTEMI: no ST-segment elevation MI. CCS: chronic coronary syndrome. BMI: body mass index. LVEF: left ventricular ejection fraction. ACE: angiotensin converting enzyme. A2R: angiotensin 2 receptor. AHA: American heart association. ACC: American college of cardiology. RMS: resorbable magnesium scaffold. IVUS: intravascular ultrasonography. OCT: optical coherence tomography.

Steering Committee evaluated the outcomes of the patients enrolled until November 2021 to determine whether to continue or terminate recruitment. The findings of this analysis are the object of the present manuscript. Continuous data were tested for normal distribution using the Kolmogorov-Smirnov test. Values that were normally distributed were presented as mean ± standard deviation (SD), while non-normally distributed values were presented as median values and interquartile range [IQR]. Categorical variables were summarised in terms of counts and percentages. For the comparison between groups, *t*-test, Mann-Whitney *U* test and Pearson's $\chi 2$ test were applied as appropriate. The cumulative rate of the primary endpoint was estimated using the Kaplan-Meier method. To more effectively evaluate and describe differences between early and late adverse events, we performed analyses with the landmark set at 1 year. Clinical and angiographic variables (Table 1) were evaluated for predictive value by fitting a generalized linear mixed-effects multiple-variable regression model by backward elimination. To account for the non-independence of lesions, patient identification was included as a random effect in the multilevel model and the model was fitted with random intercepts. The models were fitted using maximum likelihood, and Student's *t*-tests used Satterthwaite's method. Independent predictors ($p < 0.05$) were used in the time-to-event analysis, and a Cox regression model with robust variance was fitted to account for a possible lesion correlation. Tests for proportional hazards of each covariate were based on scaled Schoenfeld residuals. In order to perform propensity matching, the following parameters were considered relevant based on prognostic role and availability in the ARYOSTO and SHERPA-MAGIC databases: age, sex, diabetes, ST-segment elevation MI, prior MI, prior PCI, left ventricle ejection fraction, multivessel disease, multivessel PCI, and year of enrolment. A greedy algorithm based on local optimization using a caliper of 0.2 was used to match each patient in the SHERPA-MAGIC study with a patient in the ARYOSTO study. One- or two-tailed tests were used as appropriate, and statistical significance was defined as $p < 0.05$. All analyses were performed using R version 3.5.1 (R Foundation for Statistical Computing, Vienna, Austria) by an independent statistician. Kaplan-Meir curves were generated with STATISTICA 7 (StatSoft GmbH, Hamburg, Germany).

3. Results

From December 2017 to November 2021, 568 patients were enrolled in the study. Thirteen (2.3%) patients were excluded as they were treated with a different BRS. Five (0.9%) cases were not considered because RMS was implanted in overlap with DES due to an operator decision. In seven (1.2%) cases, RMS implantation failed. Despite adequate pre-dilatation and buddy wire, it was not possible to deliver it on the target lesion, and then the operator preferred to switch to DES implantation. The final study population consisted of 543 patients (Table 1). The mean age was 56 ± 9 years. The most common clinical presentation was MI ($n = 402$, 74%). The adherence and distribution of the prespecified criteria for patient selection are shown in Fig. 1.

3.1. Target vessels and RMS implantation

Overall, 635 diseased vessels were treated with a total of 866 RMS. The procedural data and quantitative coronary angiography (QCA) analyses are presented in Table 1. The most frequently involved vessel was the left anterior descendent (LAD) (57%). The suggested implantation technique was followed in 96% of the cases, with 99% post-dilatation with non-compliant balloon. In 45 (7.1%) cases, the operator has to change the guiding catheter or to perform deep intubation technique or to use a buddy wire to facilitate RMS deployment.

3.2. Vessel-oriented outcome

The median follow-up was 3.5 [2.6–4.3] years, ranging from a

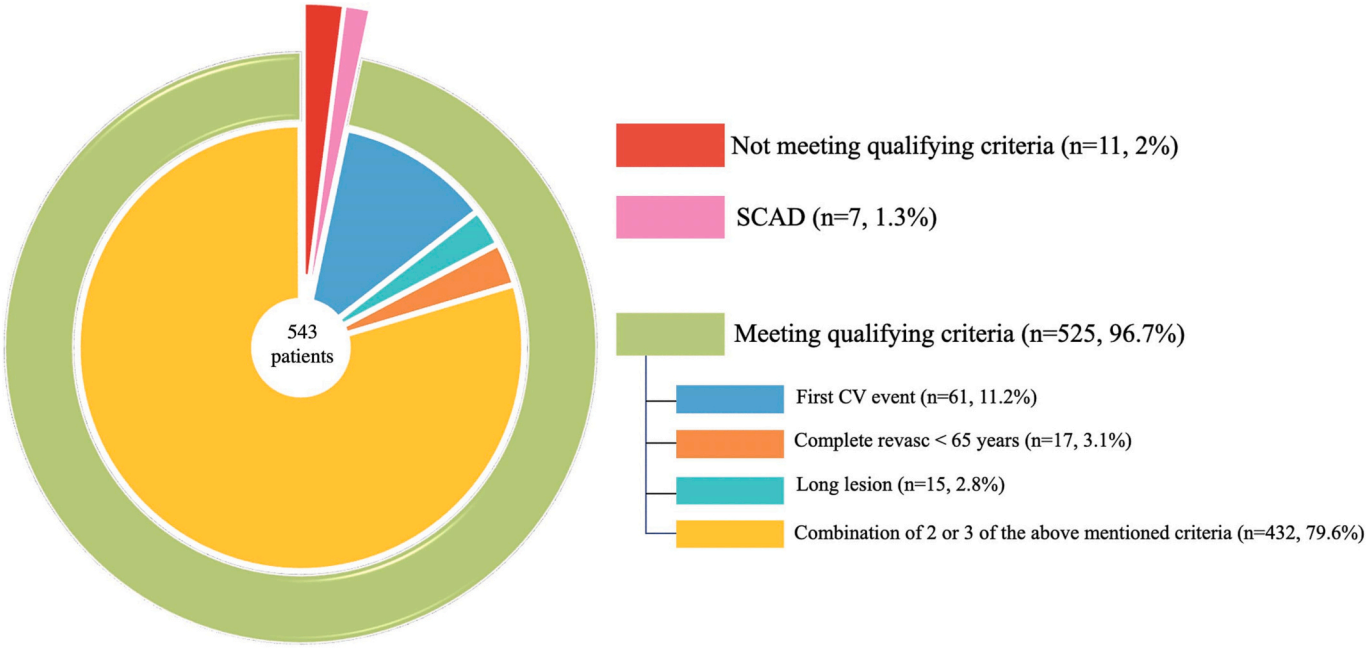

Fig. 1. Adherence and distribution of the qualifying clinical criteria for patient selection.

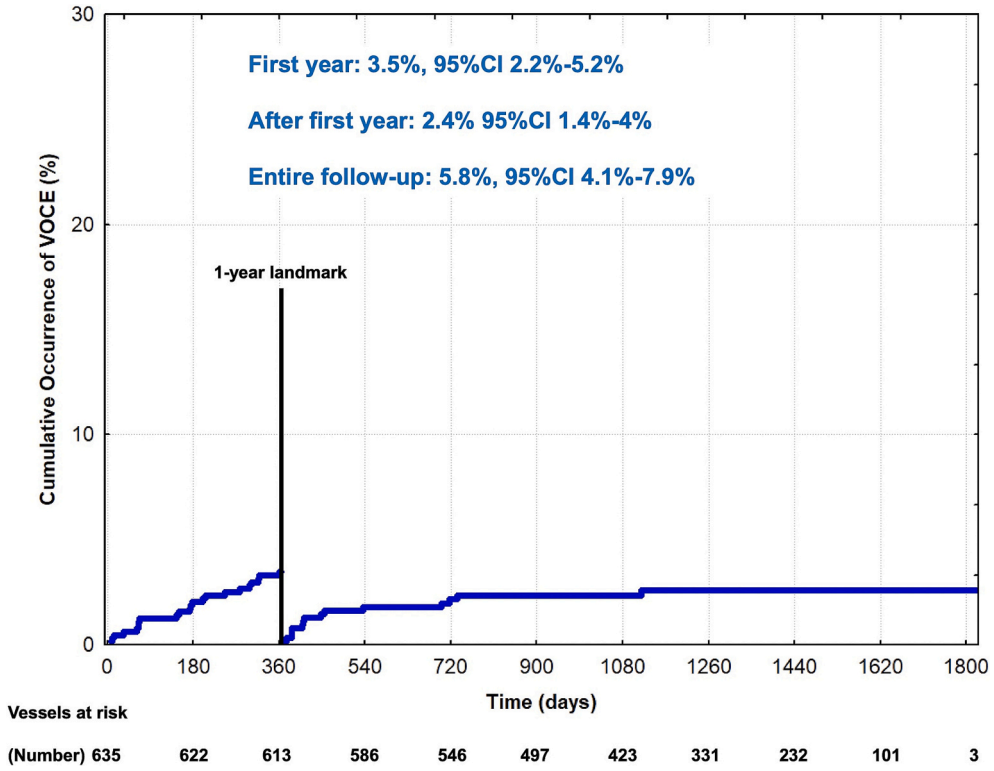

Fig. 2. Cumulative occurrence of adverse events at vessel-level.
Landmark analysis at 1 year.
VOCE: vessel-oriented composite endpoints.

minimum of 1 year to a maximum of 5 years. At 1-year, we observed 1 (0.2%) cardiac death, 11 (1.7%) TVMI and 21 (3.3%) id-TVR in the study vessels treated with RMS. The 1-year cumulative occurrence of VOCE was 22 (3.5%, 95%CI 2.2%–5.2%), which was significantly lower than the prespecified primary endpoint estimation (from 5.5% to 8.5%) (Fig. 2). After the first year, 15 (2.4%, 95%CI 1.4%–4%) adverse events were observed (2 cardiac death, 1 TVMI, and 13 id-TVR) (Fig. 2). Altogether, 37 (5.8%, 95%CI 4.1%–7.9%) VOCE were detected. Instent restenosis was reported in 20 (3.1%, 95%CI 1.9%–4.8%) vessels. In 11 (1.7%) cases the instent restenosis was diagnosed in the first year. Scaffold thrombosis occurred in 4 (0.6%, 95%CI 0.1%–1.6%) cases, with one case classified as subacute, two as late and one as very late. Subacute

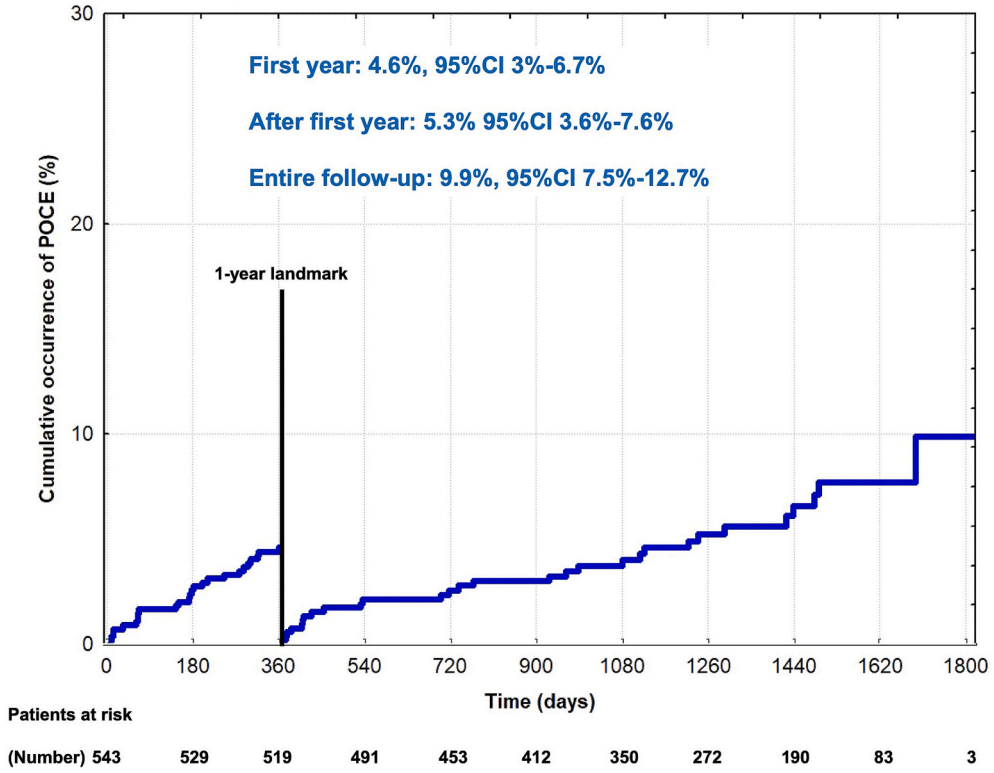

Fig. 3. Cumulative occurrence of adverse events at patient-level.
Landmark analysis at 1 year.
POCE: patient-oriented composite endpoints.

and one late scaffold thrombosis occurred during dual antiplatelet therapy. The other late scaffold thrombosis occurred after ticagrelor suspension due to severe gastrointestinal bleeding requiring blood transfusion and colonoscopy. The very late scaffold thrombosis occurred after antiplatelet interruption due to non-cardiac surgery (25 months after index procedure). Among the variables listed in Table 1, prior cardiovascular event (MI and/or PCI), clinical presentation as MI (STEMI or NSTEMI), and lesion length were independent predictors of the VOCE. The time-to-event analysis confirmed the association among prior cardiovascular event (HR 2.3, 95%CI 1.4–3.7), MI at hospital admission (HR 2.1, 95%CI 1.2–4.5), and VOCE.

3.3. Patient-oriented outcomes

At 1-year, 2 (0.3%) patients died, 13 (2.4%) experienced MI, and 23 (4.2%) underwent coronary revascularization, for a total of 25 (4.6%, 95%CI 3%–6.7%) POCE. After the first year, 7 (1.3%) deaths, 5 (0.9%) MI, and 19 (3.5%) revascularizations occurred, for a total of 29 (5.3%, 95%CI 3.6–7.6%) POCE. Altogether, at the longest follow-up, 54 (9.9%, 7.5%–12.7%) patients met criteria for POCE (Fig. 3).

3.4. Propensity score-matched analysis in MI populations

Table 2 shows the propensity matched MI populations. We did not find significant differences in the cumulative occurrence of POCE (SHERPA-MAGIC 11.4% vs. ARYOSTO 12.5%, $p = 0.71$). The finding was consistent also after stratification for 1-year landmark set (Fig. 4).

4. Discussion

The SHERPA-MAGIC study prospectively collected data from consecutive patients who underwent RMS implantation in different Italian centres. This study has four major strengths. First, the agreement and sharing of clinical criteria for patient selection and standardization of implantation technique among participating centres and operators. Second, a median follow-up of 3.5 years to investigate the long-term outcome of RMS. Third, the adverse events were centrally evaluated and attributed to the relevant vessels, enabling both vessel- and patient-level analysis, as well as the ability to accurately discern adverse events related to RMS. Fourth, given the concern surrounding the treatment of MI patients with RMS, we specifically addressed this issue by comparing MI patients in the SHERPA-MAGIC trial to a contemporaneous matched population of MI patients treated with second-generation DES.

The main findings are as follows.

i. The procedure success is favourable and consistent with the literature on second-generation DES (98.7%, 95%CI 97.4%–99.4%).
ii. At vessel-level, 1-year outcomes were low (3.5%, 95%CI 2.2%–5.2%) and slightly inferior to expectations. The finding was confirmed beyond the first year, with minimal adverse events related to RMS failure.
iii. Patient-level analysis supports that at vessel-level, indicating that the majority of events in the first year are attributable to target vessels, whereas later events are infrequently linked to RMS.
iv. Seventy-four percent of the SHERPA-MAGIC patients were hospitalised for MI. As expected, MI at clinical presentation was associated with an increased risk of adverse events in the follow-up. However, RMS performance was satisfactory and comparable to that of a similar cohort of MI patients treated with second-generation DES.

Currently, the majority of data on RMS performance originate from the BIOSOLVE studies [3–6]. In comparison to BIOSOLVE populations, a higher proportion of MI patients were enrolled in this study (74% vs. 19% in BIOSOLVE IV) and we did not exclude patients with ST-segment

Table 2
Propensity score-matched cohorts of patients with myocardial infarction from ARYOSTO and SHERPA-MAGIC studies.

	ARYOSTO Entire cohort (n = 2275)	ARYOSTO matched cohort (n = 402)	SHERPA-MAGIC MI cohort (n = 402)	p-value*
Age, (years)	69 ± 13	55 ± 9	55 ± 9	0.99
Male sex, no. (%)	1752 (77)	319 (79)	319 (79)	0.99
CV risk factors, no. (%)				
Diabetes	683 (30)	44 (11)	44 (11)	0.99
Hypertension	1593 (70)	210 (52)	204 (50.7)	0.72
Hyperlipidemia	1433 (63)	215 (53)	200 (50)	0.32
Current smoker	728 (32)	173 (43)	181 (45)	0.62
Medical history, no. (%)				
MI and/or PCI	660 (29)	67 (17)	67 (17)	0.99
COPD	137 (6)	10 (2)	7 (2)	0.63
PAD	205 (9)	22 (5)	19 (5)	0.74
Clinical presentation				
STEMI, no. (%)	842 (37)	163 (41)	163 (41)	0.99
NSTEMI, no. (%)	1433 (63)	239 (59)	239 (59)	
Other data				
BMI, kg/m^2	26 [24–30]	27 [24–29]	27 [24–29]	0.84
Creatinine clearance, mg/ml	81 [59–100]	115 [90–140]	118 [90–138]	0.61
LVEF (%)	51 [43–60]	56 [49–60]	56 [49–60]	0.90
Angiographic data				
Multivessel disease, no. (%)	1229 (54)	96 (24)	96 (24)	0.99
Multivessel PCI, no. (%)	478 (21)	60 (15)	60 (15)	0.99
Medical therapy, no. (%)				
Aspirin	2093 (92)	401 (99)	402 (100)	0.95
Ticagrelor/Prasugrel	1388 (61)	370 (92)	369 (92)	0.98
ACE inhibitor/A2R blocker	1820 (80)	262 (65)	255 (63)	0.66
High-potency statin	1843 (81)	380 (94)	386 (96)	0.40

MI: myocardial infarction. CV: cardiovascular. PCI: percutaneous coronary intervention. COPD: chronic obstructive pulmonary disease. PAD: peripheral artery disease. STEMI: ST-segment elevation MI. NSTEMI: no ST-segment elevation MI. BMI: body mass index. LVEF: left ventricular ejection fraction. ACE: angiotensin converting enzyme. A2R: angiotensin 2 receptor.

* p-value for the comparison between ARYOSTO and SHERPA-MAGIC matched cohorts.

elevation MI (30% of SHERPA-MAGIC cases) [6]. Additionally, the treated lesions were more complex, with longer lesion length, more AHA/ACC B2/C and bifurcation lesions, and in approximately one-third of the vessels, RMS were implanted in an overlapping fashion (vs 1% in BIOSOLVE IV) [6]. Despite the increased complexity, RMS performance was still favourable, with a percentage of 1-year adverse event rate similar to that observed in the BIOSOLVE series (3.5% in the SHERPA-MAGIC vs. 6% in the BIOSOLVE II-III and 4.3% in the BIOSOLVE IV) [3–6]. Outcomes beyond the first year further reinforce the safety and effectiveness of RMS. Comparing the vessel- and patient-level analyses, few adverse events were attributable to RMS failure, with the majority attributed to other vessels or disease progression. This observation is consistent with the report of Ueki et al. suggesting that late scaffold recoil was the major mechanism of RMS failure, and it was related to underlying plaque morphology (less frequent in cases with lipid plaques) [13]. A thorough examination of the Kaplan-Meier curves reveals that the majority of adverse events related to RMS occur within 9–15 months post-implantation, when late scaffold recoil is prevalent. Although future studies and analyses are needed to confirm it, we may speculate that the overall incidence of VOCE was low because SHERPA-MAGIC study primarily recruited mainly young MI patients with a predominance of lipid plaques that are associated with a better RMS performance. These results appear to be in contrast with the findings of the MAGSTEMI trial [14]. The MAGSTEMI trial enrolled 76 STEMI patients, whereas the SHERPA-MAGIC MI trial included 402 patients with myocardial infarction (MI), of which 163 had STEMI [14]. In the MAGSTEMI trial, follow-up coronary angiography was mandatory after one year, which may have contributed to a higher rate of target vessel revascularization (TVR). Additionally, the implantation technique was less standardized in the MAGSTEMI trial, with a lower utilization of pre-dilation (75% vs. 95%), no use of intracoronary imaging (vs. 56% in SHERPA-MAGIC), and less frequent use of post-dilation (88% vs. 99% in SHERPA-MAGIC) [14]. The MAGSTEMI study revealed a higher incidence of POCE among the RMS group in comparison to the DES group [14]. Furthermore, while the rate of adverse events within the DES arm were consistent with expectations, those within the RMS group were excessive and may be attributed to the aforementioned causes [14]. The 1-year POCE rate in the SHERPA-MAGIC MI cohort was similar to that of the DES cohort of the MAGSTEMI. Although it was a post-hoc-analysis, the same observation was supported by the comparison with the matched cohort of the ARYOSTO study. In addition, the MAGSTEMI trial suggested that the number of adverse events related to RMS is negligible after the first year, a finding that is consistent with our analysis [7].

4.1. Limitations

This analysis is based on an observational study, and therefore is subject to the limitations inherent in this type of research. The investigators included all the consecutive patients receiving RMS, but they represent a minority of the patients meeting the selection criteria specified in SHERPA-MAGIC protocol. Indeed, the decision to implant RMS was at the discretion of the operator and in many cases, despite the patient was potentially eligible for RMS implantation, the operator decided to implant a second-generation DES. The data for this study was collected from a limited number of centers ($n = 18$) sharing strict criteria for patient selection and implantation technique. Thus, the generalizability of these findings should be considered with caution and further validated. In particular, the number of patients with spontaneous coronary artery dissection is very low ($n = 7$) and RMS in this specific setting need further investigation because their use is not underpinned by robust data. In the SHERPA-MAGIC study, the use of intracoronary imaging was highly recommended. In more than half of the cases, IVUS or OCT guided the procedure with a plausible positive effect on outcomes [15]. Based on this and on previous studies, in future randomized studies intracoronary imaging should be mandatory. Finally, the data from MI patients in the SHERPA-MAGIC study are reassuring but should be considered with caution. The comparison with the matched cohort from the ARYOSTO study was not pre-specified and it cannot allow drawing definitive conclusions. Future studies should not only to assess the superiority of RMS over second-generation DES, but also to understand if the potential improvement related to RMS implantation is consistent in both stable and MI patients.

5. Conclusions

The SHERPA-MAGIC study demonstrates that a thorough patient selection process and adherence to a standardized implantation technique are associated with long-term favourable outcomes following RMS implantation. These results can serve as a useful guide for the design and implementation of future randomized clinical trials that aim to investigate the superiority of RMS over second-generation DES.

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Declaration of Competing Interest

The authors declare no conflicts of interests. All authors take

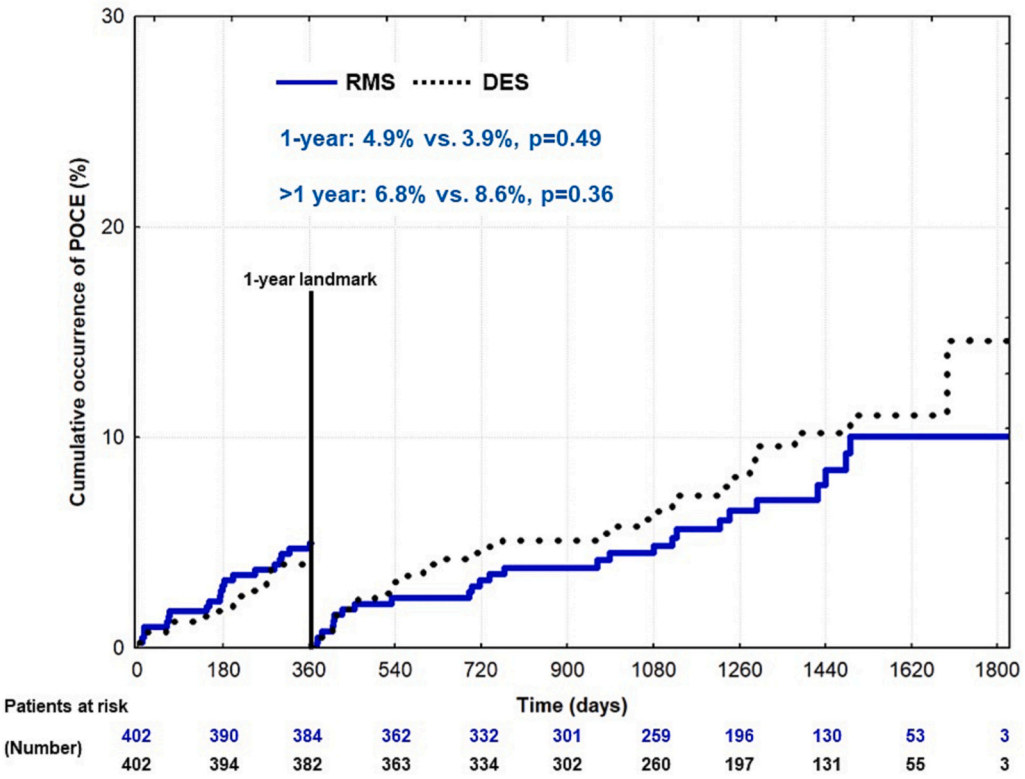

Fig. 4. Cumulative occurrence of adverse events in patients with myocardial infarction of the SHERPA-MAGIC and ARYOSTO matched cohorts. Landmark analysis at 1 year. Continue blue line: SHERPA-MAGIC cohort. Dotted black line: ARYOSTO cohort. POCE: patient-oriented composite endpoints. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation.

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