Cardiovascular Revascularization Medicine 20 (2019) 1140–1145

Contents lists available at ScienceDirect

Cardiovascular Revascularization Medicine

Magnesium 2000 postmarket evaluation: Guideline adherence and intraprocedural performance of a sirolimus-eluting resorbable magnesium scaffold☆

Adrian Wlodarczak [a,*], Luis Antonio Iñigo Garcia [b], Pasi P. Karjalainen [c], András Komócsi [d], Francesco Pisano [e], Stephan Richter [f], Magdalena Lanocha [a,g], Jose Ramón Rumoroso [h], Kwok Fai Leung [i]

[a] Department of Cardiology, MCZ Hospital, Lubin, Poland
[b] Department of Interventional Cardiology, Hospital Costa del Sol, Marbella, Malaga, Spain
[c] Department of Cardiology, Helsinki University Hospital, Helsinki, Finland
[d] Heart Institute, Medical School, University of Pécs, Pécs, Hungary
[e] Department of Cardiology, Regional Hospital U. Parini, Aosta, Italy
[f] I. Medizinische Klinik, Hegau-Bodensee-Klinikum, Singen, Germany
[g] Department of Cardiology, Poznan University of Medical Sciences, Poznan, Poland
[h] Department of Interventional Cardiology, Hospital de Galdakao (Bizkaia), Galdakao, Bizkaia, Spain
[i] Unique Medical Centre, Kowloon, Hong Kong

ARTICLE INFO

Article history:
Received 17 January 2019
Accepted 5 February 2019

Keywords:
Stable angina
Bioresorbable scaffolds
Myocardial infarction
Stent thrombosis

ABSTRACT

Background: The Magmaris bioresorbable magnesium scaffold was successfully tested in in-vitro and in clinical premarket studies. Subsequently the Magmaris postmarket program aimed to review intraprocedural data of at least 2000 patients to assess user preferences, guideline adherence and intraprocedural performance in clinical routine.

Methods: This international multicentre survey encompasses data from 356 hospitals across 45 countries. As part of the certification for Magmaris implantation, each hospital had to complete consecutive post-market evaluation forms of their first 10 commercial Magmaris patients.

Results: From June 2016 to May 2018, data on 2018 implantations were collected. Main reasons for selecting Magmaris was patients' life expectancy (67%, n = 1359) and low or not calcified lesions, (67%, n = 1357). Magmaris was successfully deployed in 99% of cases (n = 1995), predilatation was performed in 95% (n = 1922) and post-dilatation in 87% (n = 1756). Physicians rated the overall performance and the pushability as good or very good in 96% of cases (n = 1799). Guide wire friction, trackability, and conformability were rated as good or very good in 94% of cases, and crossability in 93%. The majority of patients were scheduled to receive dual antiplatelet therapy for up to 12 months.

Conclusion: Generally, implantation guidelines were adhered to and theoretical advantages of the metal scaffold observed in in-vitro tests have translated into practice with good intraprocedural performance outcomes, confirming the controlled roll-out of this novel technology into clinical practice.

Summary for annotated table of content: The Magmaris 2000 program includes the first commercial cases at each hospital. Overall, data on 2018 implantations were collected. The high rate of pre- and post-dilatation as well as other parameters confirm that generally the implantation guidelines are adhered to and the good intraprocedural performance (rated as good or very good in 96%) confirm the theoretical advantages of a metallic scaffold in practice.

1. Introduction

Bioresorbable scaffolds (BRS) have been developed to provide temporary vessel support, to dissolve thereafter, and thus to overcome long-term events associated with permanent drug-eluting stents. However, the initial enthusiasm has been tempered due to elevated scaffold thrombosis rates prior to bioresorption in polymeric BRS raising corresponding safety concerns [1,2].

Abbreviations: BRS, bioresorbable scaffold; DAPT, dual antiplatelet therapy; OCT, optical coherence tomography.

☆ M. Lanocha received speaking fees from Biotronik. The other author has no conflicts of interest to declare.

* Corresponding author at: Department of Cardiology, MCZ Hospital, Ul. M. Sklodowskiej-Curie 66, 59-301 Lubin, Poland.
E-mail address: awlodarczak@mcz.pl (A. Wlodarczak).

https://doi.org/10.1016/j.carrev.2019.02.003

Table 1
Number of participating hospitals per country.

Country	# of hospitals	Country	# of hospitals	Country	# of hospitals
Australia	1	Greece	11	Poland	9
Austria	6	Hong Kong	9	Portugal	9
Belgium	3	Hungary	4	Romania	1
Brunei	1	Italy	67	Saudi Arabia	1
Bulgaria	8	Kazakhstan	3	Serbia	4
Chile	2	Latvia	2	Singapore	4
Croatia	1	Lebanon	3	Slovakia	2
Czech Republic	2	Libya	1	South Africa	2
Denmark	3	Luxembourg	1	Spain	38
Estonia	1	Malaysia	20	Sweden	2
Finland	3	Malta	1	Switzerland	8
France	13	Mazedonia	1	Thailand	3
Georgia	1	Netherlands	6	Turkey	1
Germany	93	New Zealand	1	United Arabic Emirates	1
Great Britain	1	Palestine	1	Vietnam	1

In contrast to polymeric scaffolds, the Magmaris sirolimus-eluting metal BRS (Biotronik AG, Bülach, Switzerland) is made of magnesium. It is the first clinically proven metal scaffold and has gained CE-certification in June 2016. Premarket studies such as BIOSOLVE-II and -III showed good safety and performance data with absence of definite or probable scaffold thrombosis [3,4], but post-market data are scarce. In particular, data are lacking to validate if the theoretical advantages of metal scaffolds over polymeric scaffolds seen in in-vitro tests [5] can be confirmed in clinical practice.

The Magnesium 2000 post-market evaluation was initiated to review intraprocedural performance in practice, to observe user preferences, to monitor compliance to implantation guidelines such as the "4Ps" (proper patient and lesion selection, proper sizing, predilatation and post-dilatation) [4,6], and hence to monitor a controlled roll-out of this novel device into clinical routine.

2. Materials and methods

2.1. Study design and population

This international multicentre survey planned to collected data from at least 2000 consecutive Magmaris implantations starting with the first commercial implantations in June 2016. As part of the certification process to use Magmaris, physicians needed to complete a post-market evaluation form for at least 10 cases.

There was no restriction in data collection through in- or exclusion criteria. Data were collected via anonymized post-market evaluation forms and were not monitored. Evaluated were questions related patient selection, sizing, pre- and post-dilatation, scaffold implantation, performance outcomes and planned dual antiplatelet (DAPT) use.

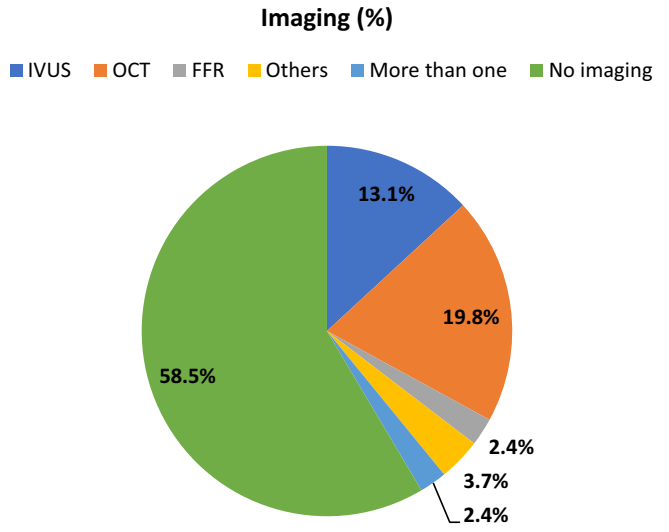

Fig. 2. Use of additional imaging techniques and functional flow reserve. FFR-functional flow reserve, IVUS-intravascular ultrasound, OCT-optical coherence tomography.

2.2. Device and procedure

Magmaris has been described previously [3,4]. It is a magnesium bioresorbable scaffold coated with BIOlute consisting of sirolimus embedded in a PLLA polymer that provides a controlled drug release up to 90 days; the scaffold absorption time is approximately 12 months.

Magmaris is available in diameters of 3.0 and 3.5 mm and lengths of 15, 20, and 25 mm. Starting in early 2017, implantation guidelines were updated to the "4P-guidelines"- Patient selection (de novo lesions with a reference vessel diameter and lesion length closely matching the available Magmaris sizes), Proper sizing (Magmaris should not be implanted in vessels <2.7 mm or >3.7 mm, if uncertain, quantitative lesion evaluation with quantitative coronary angiography, intravascular ultrasound, and/or optical coherence tomography should be performed, keeping in mind that angiograms generally underestimate the vessel diameter by 0.25 mm), Pre-dilatation (mandatory, with a non-compliant balloon with a 1:1 balloon to artery ratio, residual stenosis should be <20%, and, if this is not achieved, other balloon technologies such as

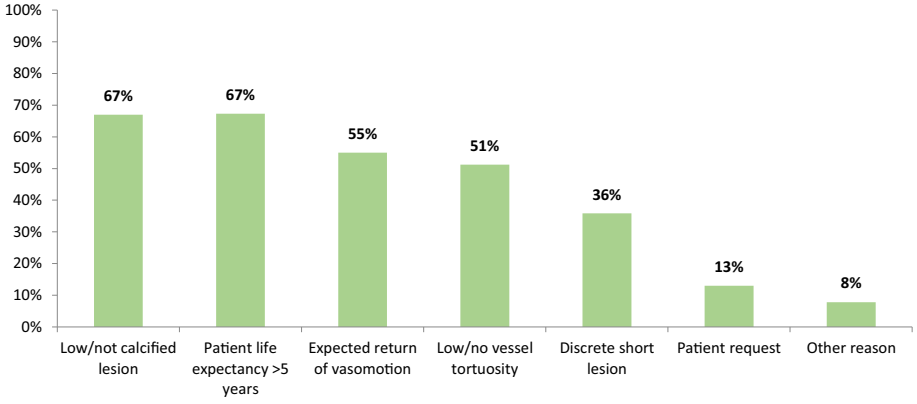

Fig. 1. Rationale for selecting Magmaris. Multiple answers were possible.

scoring balloons may be used), and post-dilatation (post-dilatation with a non-compliant balloon which is 0.5 mm larger than the implanted scaffold at high pressure >16 mm is recommended, but the expansion limit of Magmaris of 0.6 mm should be considered; optical coherence tomography is helpful to assess malappositions during the learning phase).

2.3. Statistical analysis

The analysis is based on the intention-to-treat population, defined as patients in whom the scaffold entered the guiding catheter. Further, data analysis is based on the data available. Categorical data were calculated using absolute and relative frequencies. Statistical analyses were performed with Excel Version 2010.

3. Results

From June 2016 until May 2018, 651 physicians in 356 hospitals across 45 countries in Europe, Asia, South America, Africa and Australia/New Zealand evaluated 2018 Magmaris implantations (Table 1). Of the 2018 implantations, approximately half (n = 1070) were conducted prior to the introduction of the "4P" guidelines.

The rationale to use Magmaris was patient's life expectancy of >5 years in 67% (n = 1359), low or not calcified lesions in 67% (n = 1357) and patient's preference for resorbable technologies in 13% (n = 262) (Fig. 1).

Additional imaging and functional flow reserve were used in 41% of cases (n = 837), out of which optical coherence tomography (OCT) was the preferred method (Fig. 2). Access was predominantly radial (74%, n = 1489), and the size of the guiding catheter was

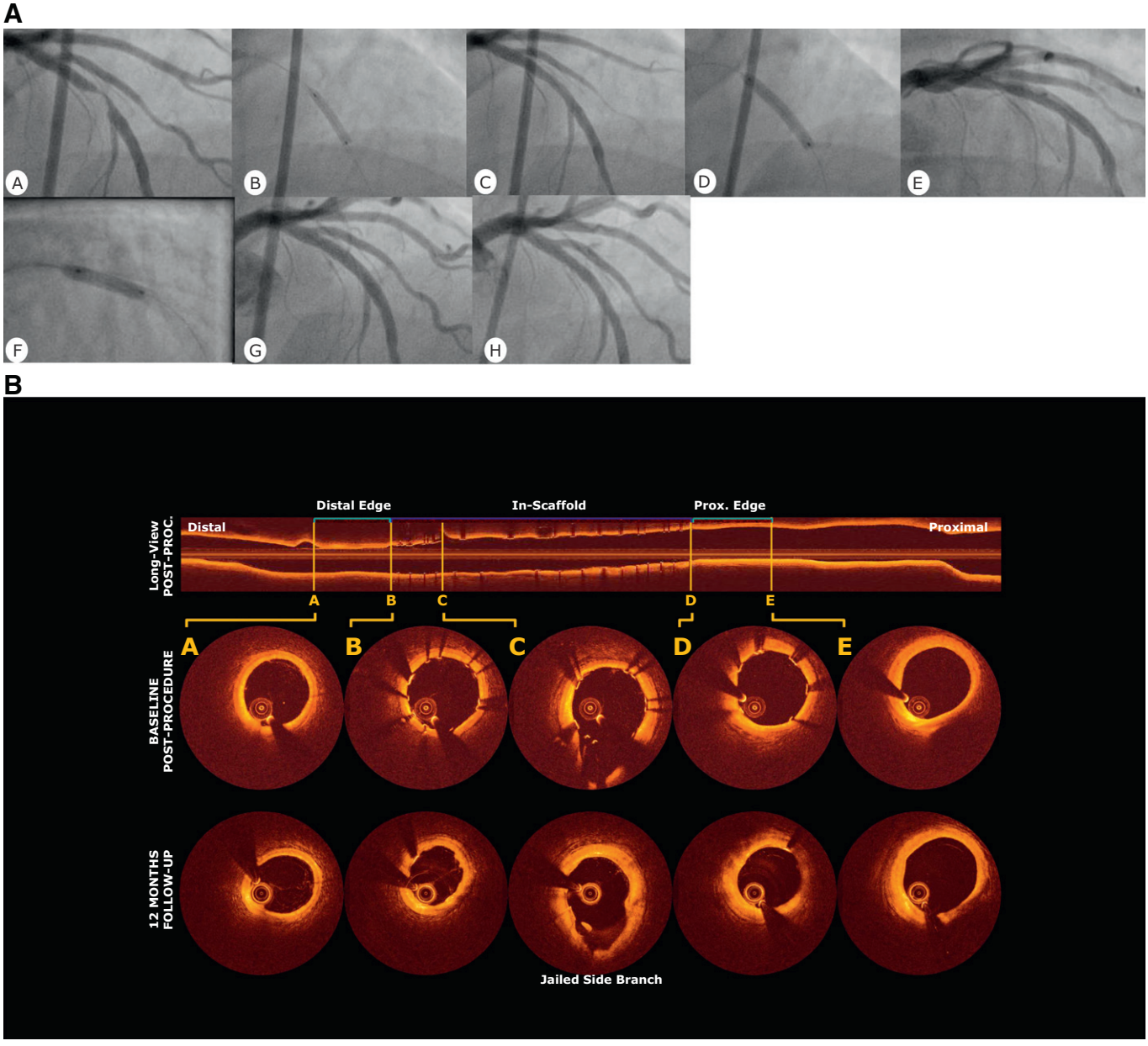

Fig. 3. Case example. (A) Angiographic assessment. A. Baseline lesion B. Predilatation with a scoring balloon, 3,5 × 15mm, at 10 atm, C. Residual stenosis <20%. D. Magmaris, 3.5 × 25mm, at 10 atm, E. Angiography post-implantation. F. Post-dilatation with a noncompliant balloon, 3,25 × 15mm, at 20 atm, G. Post-procedure: H: 12-month follow-up. (B) Optical coherence tomography (OCT) 2D post-implantation: excellent strut apposition with some struts covering the side branch OCT 2D at 12-month without visible strut remnants and struts initially covering the side branch being resorbed.

predominantly 6F (84%, n = 1669). Pre-dilatation was used in 95% of cases (n = 1922) without clear preference using a non-compliant or compliant balloon, and a second pre-dilatation was needed in 29% (551/1922). Magmaris was successfully deployed in 99% of patients (n = 1995); unsuccessful deployment was mainly due to difficulties to cross the lesion. Post-dilatation was performed in 87% (n = 1756) with a maximum pressure above 16 atm applied in 54% of recorded cases (921/1709) (Table 2). A case example is shown in Fig. 3 with angiographic and Optical Frequency Domain Imaging provided as Supplementary material.

Physicians' feedback on the performance of Magmaris is provided in Fig. 4. The performance of Magmaris was rated as good or very good in 96% of cases (n = 1799). Compared to the Absorb scaffold (Abbott Vascular, Santa Ana, CA, USA), the conformability of Magmaris was rated as better in 73% of cases, the crossability in 77%, the trackability in 74% and the pushability in 74%.

The majority of patients was planned to receive DAPT for up to 12 months (Fig. 5).

4. Discussion

The main findings of the Magmaris 2000 program were (a) in general, physicians adhered to the implantation guidelines ("4 Ps") even though these were not available in the current form at the start of the data collection and (b) the Magmaris metal scaffold showed superior intraprocedural performance outcomes compared to a polymeric scaffold, confirming results from preclinical bench testing.

4.1. Implantation guidelines - 4Ps

For BRS, adherence to implantation guidelines is paramount and results in significantly better outcomes [7]. In our series, guidelines were in general respected which resulted in 99% successful implantations despite inclusion of first-time users.

Patient selection: the majority of patients (67%) received Magmaris scaffold based on their long life-expectancy and approximately one third (36%) had discrete short lesions, both regarded as criteria for an optimal patient outcome according to a recent consensus paper [6].

Proper sizing: intracoronary imaging is recommended in case of uncertainty about the vessel diameter, furthermore, OCT is helpful to verify malapposition after scaffold implantation during the learning phase [4,6]. In more than half of the patients in this series, no additional imaging system aside of angiography was used. Considering the very early experience, a higher usage of additional images would have been desired, but it has to be acknowledged that there seems to be a trade-off to the additional costs involved.

Pre-dilatation should be performed in all patients with a non-compliant balloon to achieve a residual stenosis <20%. In our series, pre-dilatation was performed in 95% of implantations and a second predilatation in 29%, which is indicative that pre-dilatation was performed thoroughly. While a non-compliant balloon was only used in approximately half of the first pre-dilatations, they were used more frequently (63%) for second pre-dilatation, when also 17% scoring and cutting balloons were used. Those are particularly helpful for fibrotic lesions to avoid slipping of the balloon.

Post-dilatation ought to be performed with a non-compliant balloon using an inflation pressure >16 atm unless intracoronary imaging confirms good scaffold expansion [6]. The post-dilatation rate of 87% is indicative that the guidelines are adhered to, yet only 54% applied a pressure of >16 atm. The reason behind might be multifactorial. Physicians might be concerned to post-dilate too aggressively and eventually intracoronary imaging already showed good scaffold apposition with lower pressures, or physicians were used to the recommendations for polymeric scaffolds that recommend a post-dilatation using 14 to 16 atm [2]. These concerns can be alleviated through a recent multicentre analysis in 37 de novo lesions, in which OCT was performed before and after non-compliant balloon post-dilatation with 16 atm. Thereby post-dilatation led to a significantly lager mean scaffold

Table 2
Procedural characteristics.

	N = 2018
Pre-dilatation	
Pre-dilatation performed	1922/95%
Pre-dilatation balloon, n = 1922	
Non-compliant	924/48%
Semi-compliant	880/46%
Scoring/cutting balloon	19/1%
Rotablator	0/0%
Combinations[a]	99/5%
Second pre-dilatation performed, n = 1922	551/29%
Pre-dilatation balloon, n = 551	
Non-compliant	348/63%
Semi-compliant	107/19%
Scoring/cutting balloon	94/17%
Rotablator	2/<1%
Pre-dilatation time [sec], n = 1894	
≤10	632/33%
11–15	395/21%
16–20	443/23%
21–25	56/3%
26–30	300/16%
>30	68/4%
Maximum pressure applied [atm], n = 1917	
≤10	179/9%
11–15	871/45%
16–20	812/42%
21–25	33/2%
>25	22/1%
Scaffold implantation	
Magmaris sizes, n = 1934	
3.0 × 15 mm	351/18%
3.0 × 20 mm	380/20%
3.0 × 25 mm	322/17%
3.5 × 15 mm	299/16%
3.5 × 20 mm	303/16%
3.5 × 25 mm	279/14%
Inflation time [sec], n = 1974	
≤10	184/9%
11–15	237/12%
16–20	536/27%
21–25	118/6%
26–30	624/32%
>30	275/14%
Maximum pressure applied [atm], m = 1976	
≤10	273/14%
11–15	948/48%
16–20	745/38%
21–24	10/<1%
Magmaris successfully deployed	1995/99%
Post-dilatation	
Post-dilatation performed	1756/82%
Inflation time [sec], n = 1694	
≤10	516/30%
11–15	375/22%
16–20	421/25%
21–25	49/3%
26–30	270/16%
>30	63/4%
Maximum pressure applied [atm], n = 1709	
≤10	55/3%
11–15	365/21%
16–20	1106/65%
21–25	153/9%
>25	30/2%

Data are presented as n/%.
[a] e.g. Non-compliant plus scoring balloon.

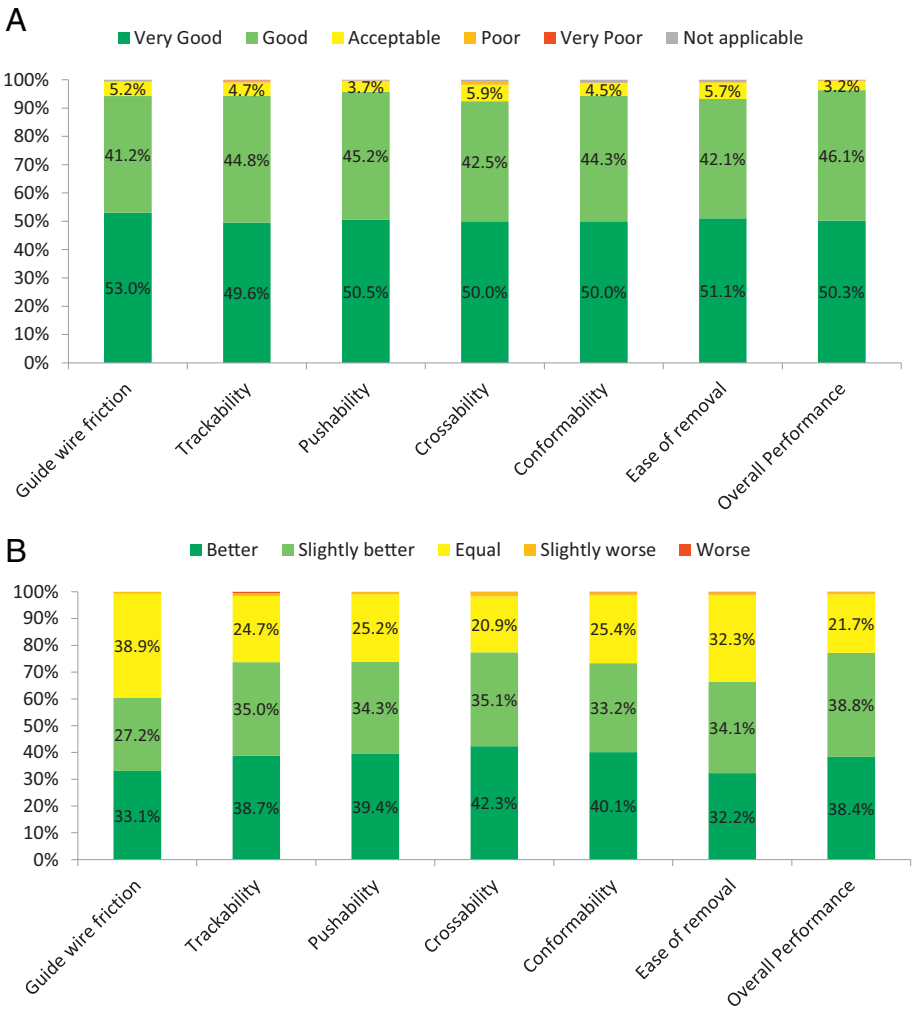

Fig. 4. Rating of intraprocedural performance. (A) Magmaris scaffold (B) Magmaris versus polymeric scaffold Per physicians' feedback. (A) Data were available for 1867 to 2000 cases, depending on the question raised (B) comparison to Absorb, data were available for 1331 to 1450 cases, depending on the question raised. Conformability: Parameter describing the difference in vessel curvature and angulation between pre and post-stent implantation. Crossability: Ability to cross tortuous vessels and narrow lesions. Trackability: Ability of a system to be advanced through a curved vessel anatomy. Pushability: Functional parameter to assess the force transfer from the proximal shaft to the very distal tip of the stent system.

diameter (Δ~0.4 mm), abluminal scaffold area (Δ~1.2 mm^2), and lumen area (Δ~0.75 mm^2), and a lower incomplete scaffold apposition area (0.01 ± 0.04 mm^2 vs. 0.17 ± 0.11 mm^2) without observation of strut fractures. Only one dissection occurred after implantation and prior to post-dilatation. These findings support the view that post-dilatation is safe and required for optimal expansion [8].

Dual antiplatelet therapy was predominantly planned for 12 months or less which corresponds to the suggestion of a recent state of the art paper to apply DAPT at least until scaffold degeneration [1], which is approximately 12 months for Magmaris.

4.2. Intraprocedural performance

Magnesium based metal-scaffolds have several theoretical advantages. (i) they achieve a good radial strength and low recoil; (ii) magnesium alloy has a higher tensile strength and elongation to break resistance compared to polymers, offering a higher compliance to the vessel geometry and lowers the risk of scaffold fracture; (iii) they can be implanted via a single-step inflation, and (iv) electropolishing of magnesium results in soft, round edges to improve trackability, deliverability and flow dynamics [1,2,9,10].

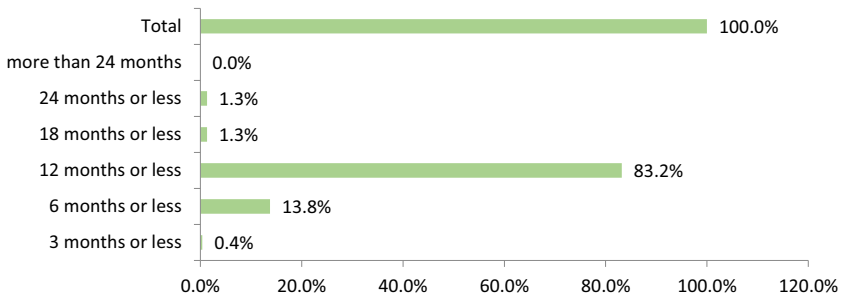

Fig. 5. Planned dual antiplatelet therapy. Data were available for 1504 cases.

These theoretical advantages have been confirmed in preclinical bench tests [5,11], but were never systematically assessed in humans. Magmaris 2000 is the first systematic assessment of intraprocedural performance criteria and confirmed that superior bench tests compared to Absorb translate into improved performance parameters in humans.

In particular, the Magmaris backbone has an up to 80% reduced bending stiffness in bench tests (means is up to 80% more flexible), compared to the polymeric Absorb scaffold [5] and correspondingly, in 73% of cases of our series, the physician rated the conformability as better or slightly better for Magmaris compared to Absorb. Magmaris also required up to 40% lower lesion entry and crossing force compared to the Absorb scaffold in bench tests [5], and correspondingly, crossability was rated as better or slightly better in 77% in our series. Trackability is the ability of the scaffold to be advanced through a curved vessel anatomy. In tortuous anatomies, Magmaris required 29% less peak force in bench tests [5], and correspondingly, in 74% of cases, the physicians rated the overall trackability as better or slightly better. High pushability provides good feedback to the user, enables safe catheter maneuvers, and an optimum pushability has a positive impact on catheter trackability. Magmaris had 34% more force transmitted from hub to tip compared to Absorb during bench testing [5], and was correspondingly rated as having a better or slightly better pushability than Absorb in 74% of cases.

The overall performance of Magmaris was rated as good or very good in 96% of patients even though Magmaris, as other scaffolds, has substantially thicker struts compared to modern drug-eluting stents to which physicians are accustomed to. This rating might reflect the general knowledge gained through polymeric scaffolds, the Magmaris training program that prepares physicians for their first implantations, or that the Magmaris implantation feels like that of a metallic device and hence is more comparable to permanent drug-eluting stents than to polymeric scaffolds.

Our analysis has several limitations. Data were not monitored and physicians' assessment might have been biased through the enthusiasm of the first use of this novel product. Data comparing Magmaris with Absorb were missing in >25% of cases. Furthermore, no safety or long-term data were provided. Nevertheless, this is the largest series of Magmaris implantations to date and its strength is the assurance that the first consecutive patients were reported.

5. Conclusions

In >2000 implantations outside of clinical trials, implantation guidelines were generally adhered to. The implantation of Magmaris resulted in excellent acute performance outcomes confirming the results of bench tests comparing Magmaris to the leading polymeric scaffold and demonstrating that Magmaris performs better in terms of deliverability (trackability, pushability and crossability), but also in terms of conformability.

Supplementary data to this article can be found online at https://doi.org/10.1016/j.carrev.2019.02.003.

Acknowledgements

We thank Beatrix Doerr, for her medical writing assistance reimbursed by Biotronik AG.

Funding

This work was supported by Biotronik AG, Buelach, Switzerland.

References

[1] Katagiri Y, Stone GW, Onuma Y, Serruys PW. State of the art: the inception, advent and future of fully bioresorbable scaffolds. EuroIntervention 2017;13:734–50.
[2] Sotomi Y, Onuma Y, Collet C, Tenekecioglu E, Virmani R, Kleiman NS, et al. Bioresorbable scaffold: the emerging reality and future directions. Circ Res 2017;120:1341–52.
[3] Haude M, Ince H, Kische S, Abizaid A, Tölg R, Lemos PA, et al. Sustained safety and clinical performance of a drug-eluting absorbable metal scaffold up to 24 months: pooled outcomes of BIOSOLVE-II and BIOSOLVE-III. EuroIntervention 2017;13:432–9.
[4] Haude M, Ince H, Kische S, Abizaid A, Tölg R, Alves Lemos P, et al. Safety and clinical performance of a drug eluting absorbable metal scaffold in the treatment of subjects with de novo lesions in native coronary arteries: pooled 12-month outcomes of BIOSOLVE-II and BIOSOLVE-III. Catheter Cardiovasc Interv 2018. https://doi.org/10.1002/ccd.27680 [Epub ahead of print].
[5] Schmidt W, Behrens P, Brandt-Wunderlich C, Siewert S, Grabow N, Schmitz KP. In vitro performance investigation of bioresorbable scaffolds - standard tests for vascular stents and beyond. Cardiovasc Revasc Med 2016;17:375–83.
[6] Fajadet J, Haude M, Joner M, Koolen J, Lee M, Tölg R, et al. Magmaris preliminary recommendation upon commercial launch: a consensus from the expert panel on 14 April. EuroIntervention 2016;12:828–33.
[7] Puricel S, Cuculi F, Weissner M, Schmermund A, Jamshidi P, Nyffenegger T, et al. Bioresorbable coronary scaffold thrombosis: multicenter comprehensive analysis of clinical presentation, mechanisms, and predictors. J Am Coll Cardiol 2016;67:921–31.
[8] Blachutzik F, Achenbach S, Tröbs M, Marwan M, Weissner M, Nef H, et al. Effect of non-compliant balloon postdilatation on magnesium-based bioresorbable vascular scaffolds. Catheter Cardiovasc Interv 2018. https://doi.org/10.1002/ccd.27794 [Epub ahead of print].
[9] Iqbal J, Onuma Y, Ormiston J, Abizaid A, Waksman R, Serruys P. Bioresorbable scaffolds: rationale, current status, challenges, and future. Eur Heart J 2014;35(12):765–76.
[10] Haude M, Ince H, Abizaid A, Toelg R, Lemos PA, von Birgelen C, et al. Safety and performance of the second-generation drug-eluting absorbable metal scaffold in patients with de-novo coronary artery lesions (BIOSOLVE-II): 6 month results of a prospective, multicentre, non-randomised, first-in-man trial. Lancet 2016;387(2):31–9.
[11] Grogan JA, Leen SB, McHugh PE. Comparing coronary stent material performance on a common geometric platform through simulated bench testing. J Mech Behav Biomed Mater 2012;12:129–38.