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ABSTRACT

Background: Balloon uncrossable coronary lesions are lesions that cannot be crossed with a conventional balloon. Multiple balloons have been designed to overcome this problem. The Blimp balloon has a very low scoring profile (0.6 mm) with a very high rated burst pressure (30 atmospheres). We aimed to evaluate the efficacy of this balloon compared to customary low-profile balloons.

Methods: We conducted a multicenter, prospective, randomized, controlled trial in which 126 patients with an uncrossable lesion were randomly (1:1 randomization) assigned to treatment first with the Blimp balloon or low-profile balloon. The primary endpoint was the success of crossing the lesion after initial failure with a microcatheter (group A) or with a conventional balloon (group B).

Results: Overall, the first attempt of Blimp was successful in 29 out of 61 cases (48%) while the LP balloon immediately crossed in 30 out 67 cases (45%;

p=0.761). Using a low-profile balloon in the BLIMP group after failure of the Blimp balloon increased the success to 64% (39 out of 61 cases). Using the Blimp balloon in the low-profile first group after failure of the low-profile balloon increased the success to 60% (40 out of 67 cases). After the placement of a guide catheter extension, the overall successful lesion crossing in the BLIMP group was 80% (49 out of 61 cases) compared to 76% (51 out of 67 cases) in the LP Balloon group (p=0.327).

Conclusions: The Blimp balloon catheter showed no superiority to customary low-profile balloons in uncrossable lesions. It can however be complementary in treating uncrossable lesions.

1 INTRODUCTION

Percutaneous coronay intervention (PCI) has become a cornerstone in the treatment of patients with coronary artery disease, presenting with acute and chronic coronary syndromes. A successful procedure requires crossing the coronary lesion with a wire followed by dilatation and stent implantation. Some lesions that are crossed with a wire, unfortunately, cannot be crossed with a conventional balloon or microcatheter. The incidence of so-called “uncrossable lesions” is estimated at 2-10% of lesions, depending on the subset studied (non-chronic total occlusion versus chronic total occlusions (CTO)).[1,2,3,4] Medical

device companies strive to improve the crossing profiles of the different devices available on the market. One of these novel devices is the Blimp balloon (IMDS, the Netherlands). The Blimp is the lowest profile scoring balloon (0.6 mm) with the highest rated burst pressure (30 atmospheres (ATM)) developed specifically to cross uncrossable lesions and prepare these lesions for further dilation and treatment. The aim of the BLIMP study is to assess, in a randomized fashion, the potential additional value of this miniscoring balloon versus current low-profile (LP) balloons.

2 MATERIALS AND METHODS

2.1 Device description: Blimp Balloon catheter

The Blimp Balloon Catheter is a rapid exchange single use device (Figure 1). With an inflated balloon diameter of 0.6 mm, the Blimp is the smallest balloon catheter in the world at this time. With a rated burst pressure of 30 ATM, the Blimp is the highest rated burst pressure balloon compared to balloons with diameters of 1.5 mm or smaller. With the rapid exchange (Rx) port only extending over the distal tip section, the guidewire creates a scoring element over the balloon. Such scoring elements create approximately four times the amount of Maximum Principle Stress on the vessel compared to the same size regular balloon catheter.[5] At the rated burst, Blimp can create a principle stress equivalent to 160 ATM. The very short Rx section whereby the guidewire forms

a scoring element over the balloon furthermore enables wedging if the balloon does not cross directly. The balloon body has, as with all balloon catheters, a larger profile. Therefore, the balloon body is less likely to cross the lesion than the distal tip. If the Blimp balloon is inflated with only a fraction of the distal tip of the balloon wedged inside the lesion/ proximal cap, it is possible that the guidewire/ scoring element at high inflation pressure will start to modify the lesion/cap resulting in subsequent full lesion entry of the body of the Blimp balloon.

2.2 Study population and design

In this multicenter randomized controlled trial, a total of 128 patients with balloon or microcatheter uncrossable lesions were enrolled (ClinicalTrials.gov Identifier NCT03947398).

For the purpose of this study, an uncrossable lesion was defined as lesions that could not be crossed with a balloon or microcatheter after successful guidewire crossing. In this scenario, the patient was subsequently randomly (1:1 randomization) assigned to treatment first with the Blimp balloon or LP balloon. Two types of lesions (“group A” or “group B”) were selected for the study. In group A, the guidewire crossed the lesion but the microcatheter did not cross (often a CTO lesion). In group B, a conventional balloon catheter (> 1.5 mm outer

diameter, OD) would not cross the lesion, with no microcatheter being used upfront (often a subtotal calcified, non-CTO lesion). The following steps were applied (Figure 2):

Firstly, patients were randomized (1:1) to a current first choice LP balloon (≤ 1.5 mm OD) ("LP Balloon first group") or to the Blimp ("BLIMP first group"). Secondly, if the first-choice LP balloon did not cross, the Blimp was subsequently used and vice versa. Thirdly, if the second step was not successful, a guide catheter extension was added and the sequence of the first step and, if needed, the second step was repeated. Finally, if the third step was also not successful, the operator was free to use any other technique to try to prepare and cross the lesion (e.g., tornus, balloon rupture, "carlino", rotablation, laser, subintimal crossing or dilation…).

Acute success or failure of crossing were reported. The study was approved by the Ethical Committees from the different hospitals participating in the trial and all patients provided written informed consent.

2.3 Study endpoints

Primary endpoint was the superiority ($P<0.05$) of the Blimp balloon to current LP balloon catheters (balloon ≤ 1.5 (mm)) in initial crossing after failure of a conventional balloon or a microcatheter to cross a coronary lesion.

Secondary endpoints were successful crossing of the Blimp balloon where current LP balloon catheters (Balloon OD ≤ 1.5 (mm)) failed with (group A) or without (group B) use of a microcatheter and procedural success defined as adequate lesion dilatation and stent placement with residual stenosis <20%.

2.4 Statistical analysis

Based on the study setup, at the inclusion rate of 128 patients, a minimum of 60 patients will have been treated with the Blimp. Under the assumption that current LP balloon catheters will have a 60% success of crossing after initial failure of a microcatheter crossing and expecting a 80% success rate for Blimp, with a power of 80%, 120 patients were required to demonstrate statistical significance between the groups.

All statistical analyses were performed with SPSS, version 25.0 (SPSS Inc, Chicago, USA). Normality was tested using the Kolmogorov-Smirnov test. Categorical variables are expressed as numbers with percentages. Continuous data are shown as mean ± standard deviation. Categorical data were compared using a Chi-Square test. Continuous data between groups were compared with the independent Student's T-test. P-values < 0.05 were considered as statistically significant.

3 RESULTS

3.1 Baseline characteristics

Overall, 128 patients were randomized, of whom 67 (52%) were allocated to apply a LP balloon first and 61 (48%) were randomized to the use of a Blimp balloon first. An overview of demographics and lesion characteristics is shown in Table 1.

In total, 79 (62%) patients were in group A, were a microcatheter initially did not cross, and 49 (38%) patients were in group B, where a microcatheter was not used and a regular balloon did not pass the lesion. Sixty-six (52%) patients had a CTO lesion, while 62 (48%) had a subtotal occlusion.

3.2 Successful crossing across the overall study population (n=128)

The success rate per crossing attempt is shown in Figure 2 for the entire study population. Overall, the first attempt of Blimp was successful in 29 out of 61 cases (48%) while the LP balloon immediately crossed in 30 out 67 cases (45%; p=0.761). After an initial failure, a LP balloon was used in those patients randomized to the BLIMP group and vice versa. Prior to the implementation of a guide catheter extension, the overall successful lesion crossing was 64% in the BLIMP group (39 out of 61 cases) compared to 60% (40 out of 67 cases) in the LP Balloon group (p=0.236). Guide catheter extension was used per protocol in 19

patients in the BLIMP group and 22 patients in the LP balloon group. After the placement of a guide catheter extension, the overall successful lesion crossing in the BLIMP group was 80% (49 out of 61 cases) compared to 76% (51 out of 67 cases) in the LP Balloon group (p=0.327).

Finally, a Blimp and/or a LP balloon could not cross the lesion in 28 (23%) cases, despite guide catheter extension support. No additional techniques were applied in 9 out of these 28 cases (at the discretion of the operator). In 19 cases, additional techniques were applied to cross which resulted in 15 successful procedures (successful techniques: Rotablation (n=6), proximal shockwave (n=1), sub-intimal tracking (n=2), switch to Turnpike Gold (n=3), switch to a Turnpike Spiral (n=1) and Laser (n=2)).

3.3 Successful crossing rate in Group A (n=79)

In this group, the first attempt of Blimp was successful in 17 out of 39 cases (44%), while the LP balloon immediately crossed in 18 out 40 cases (45%; p=0.901). After an initial failure, a LP balloon was used in those patients randomized to the BLIMP group and vice versa. This led to ,prior to the implementation of a guide catheter extension, an overall successful lesion crossing of 62% in the BLIMP group (24 out of 39 cases) compared to 63% (25 out of 40 cases) in the LP Balloon group (p=0.928). In total, 14 patients in the

BLIMP group and 14 patients in the LP Balloon group received per protocol guide catheter extension. After the placement of a guide catheter extension, the overall successful lesion crossing in the BLIMP group was 79% (31 out of 39 cases) compared to 73% (29 out of 40 cases) in the LP Balloon group (p=0.523).

3.4 Successful crossing rate in Group B (n=49)

In this group, the first attempt of Blimp was successful in 12 out of 22 cases (54%), while the LP balloon immediately crossed in 12 out 27 cases (44%; p=0.486). After an initial failure, a LP balloon was used in those patients randomized to the Blimp group and vice versa. Prior to the implementation of a guide catheter extension, the overall successful lesion crossing was 68% in the BLIMP group (15 out of 22 cases) compared to 56% (15 out of 27 cases) in the LP Balloon group (p=0.373). In total, 19 patients in the BLIMP group and 22 patients in LP Balloon received per protocol guide catheter extension. After the placement of a guide catheter extension, the overall successful lesion crossing in the BLIMP group was 82% (18 out of 22 cases) compared to 81% (22 out of 27 cases) in the LP Balloon group (p=0.979).

3.5 Procedural success rate

In total, 114 out of 128 (89%) procedures were successful. The overall procedural success rate in the BLIMP group (52 out of 61 cases (85%)) did not differ from the overall procedural success rate in the LP Balloon group (62 out of 67 cases (93%), p=0.189).

In group A (n = 79), 39 (49%) patients were randomized to the BLIMP group and 40 (51%) patients to the LP Balloon group. Within group, A, the overall procedural success rate in the BLIMP group was 82% (32 out of 39 cases) compared to a procedural success rate of 93% (37 out of 40 cases) in the LP Balloon group (p = 0.164), irrespective of the use of a guide catheter extension.

In group B (n = 49), 22 (45%) patients were randomized to the BLIMP group and 27 (55%) patients to the LP Balloon group. Within group B, the overall procedural success in the BLIMP group was 91% (20 out of 22 cases) compared to a procedural success rate of 93% (25 out of 27 cases) in the LP Balloon group (p = 0.798), irrespective of the use of a guide catheter extension.

3.6 Adverse events

Across the entire study population, only one in-hospital adverse event was reported (0.8%). Despite a successful procedure, the patient demised 4 hours after the procedure due to a spontaneous intracranial hemorrhage. No other in-hospital events were reported following any procedure.

4 DISCUSSION

4.1 Main results

This multicenter randomized controlled study is the first to evaluate the performance of the new Blimp balloon and reports on successful crossing with the Blimp balloon versus LP (≤ 1.5 mm) balloons. The Blimp balloon has the lowest crossing profile on the market and can be used at much higher pressures compared to conventional LP balloons.

In this study, complex lesion subsets were included with more than half consisting of CTO lesions, and just under half being subtotal non-CTO lesions. In 62% of lesions a microcatheter did not cross, and in 38% a regular (> 1.5 mm) semicompliant balloon did not cross the lesion. Indication to use a microcatheter up-front probably relates to the intention to exchange the dedicated high tip load CTO wire for a workhorse wire or to cross the lesion and exchange the initial wire for a rotawire.

The Blimp balloon was not superior to current conventional LP balloons in crossing CTO and complex non-CTO lesions, with or without the use of a guide catheter extension.

Expectations for Blimp, a 20% difference in crossing lesions compared to current generation LP balloons, might have been too high. Especially when adding a

guide catheter extension to increase support, current LP balloons perform very well in crossing lesions. In only 23% of the procedures, the LP or the Blimp balloon with or without guide catheter extension could not cross the uncrossable lesion, after which other microcatheters (like turnpike spiral, turnpike gold), laser, rotablation (wiring was performed with the rotawire from the tip of the microcatheter which did not fully cross the lesion) were used for crossing, dilation and treatment. Only 10% of these non-crossable lesions could not be treated (aborting the procedure was at the discretion of the operator), which is comparable to data from two large series.[3,4]

The operators found that if the lesions were not funnel-shaped, the Blimp balloon had a tendency to move towards the vessel wall instead of “tipping in” the lesion, probably because only a very small portion of the tip is guided and supported by the wire. Adding a guide extension catheter, as far as possible, and probably smaller than 6F might be used to direct the Blimp towards the lesion and limit its side ward movement. Another option would be to redesign the tip, with a longer portion of the tip being supported by the wire, but this needs to be studied in models and subsequently evaluated in clinical settings.

4.2 Limitations

A possible limitation for assessing the Blimp performance in this fashion is that when the Blimp is wedged into a lesion and inflated to high pressures, a certain degree of lesion preparation is performed. Although the “used” Blimp may then not have crossed the lesion, a new LP balloon may then have had an increased chance of crossing. This may have had a negative impact on the Blimp balloon using the endpoints defined in this study.

5 CONCLUSION

Balloon uncrossable lesions are a challenging obstacle in interventional cardiology. Different techniques can lead to successful percutaneous treatment of such lesions. The Blimp Balloon Catheter is a low profile scoring balloon (0.6 mm) with the highest rated burst pressure (30 atmospheres (ATM) developed to cross and dilate uncrossable lesions. Despite the lack of superiority, this study proofs the Blimp balloon as a valuable alternative to conventional LP balloons in the treatment of balloon uncrossable lesions.

REFERENCES

1. Pagnotta P, Briguori C, Mango R et al. Rotational atherectomy in resistant chronic total occlusions. Catheter Cardiovasc Interv 2010;76:366-71.

2. Stone GW, Colombo A, Teirstein PS et al. Percutaneous recanalization of chronically occluded coronary arteries: procedural techniques, devices, and results. Catheter Cardiovasc Interv 2005;66:217-36.

3. Patel SM, Pokala NR, Menon RV et al. Prevalence and treatment of "balloon-uncrossable" coronary chronic total occlusions. J Invasive Cardiol. 2015 Feb;27(2):78-84.

4. Karacsonyi J, Karmpaliotis D, Alaswad K et al. Prevalence, indications and management of balloon uncrossable chronic total occlusions: insights from a contemporary multicenter US registry. Catheter Cardiovasc Interv. 2017;90(1):12-20.

5. Kawase Y, Saito N, Watanabe S et al. Utility of a scoring balloon for a severely calcified lesion: bench test and finite element analysis. Cardiovasc Interv Therapy 2014 Apr;29(2):134-9.

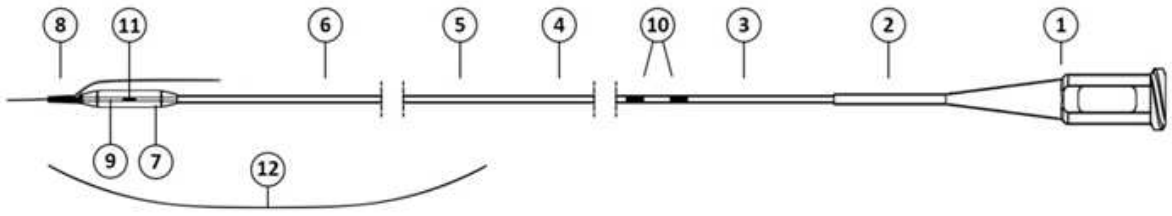

FIGURE 1 Blimp balloon catheter. The catheter consists of a hub (1) and strain relief (2), a proximal hypo tube (3), a hypo tube shaft (4), a proximal shaft (5), a distal shaft (6), an expandable balloon (7) and a distal tip (8) containing the rapid exchange guide wire section. The hub and distal tip are connected via a stiffening wire (9). On the shaft depth markings (10) are applied to indicate that the distal tip of the catheter is at the level of the distal tip of the guiding catheter (95 and 105 cm). As aid in positioning the balloon a radiopaque marker (11) is positioned in the balloon to make the balloon visible with fluoroscopy. The distal part of the shaft is fitted with a hydrophilic coating (12).

Demographics	**BLIMP (n=61)**	**Low-profile balloon (n=67)**	**P-value**
Age (in years)	69±12	67±11	0.368
Former or current smoker	38 (62)	40 (60)	0.753
Renal failure	30 (49)	28 (42)	0.402
Post-CABG	8 (13)	16 (24)	0.110
Lesion characteristics			
Blunt cap	16 (26)	18 (27)	0.975
Severe calcification	40 (66)	37 (55)	0.232
Length>20mm	23 (38)	30 (45)	0.417
Bend>45°	8 (13)	15 (22)	0.160

TABLE 1 Demographics and lesion characteristics.

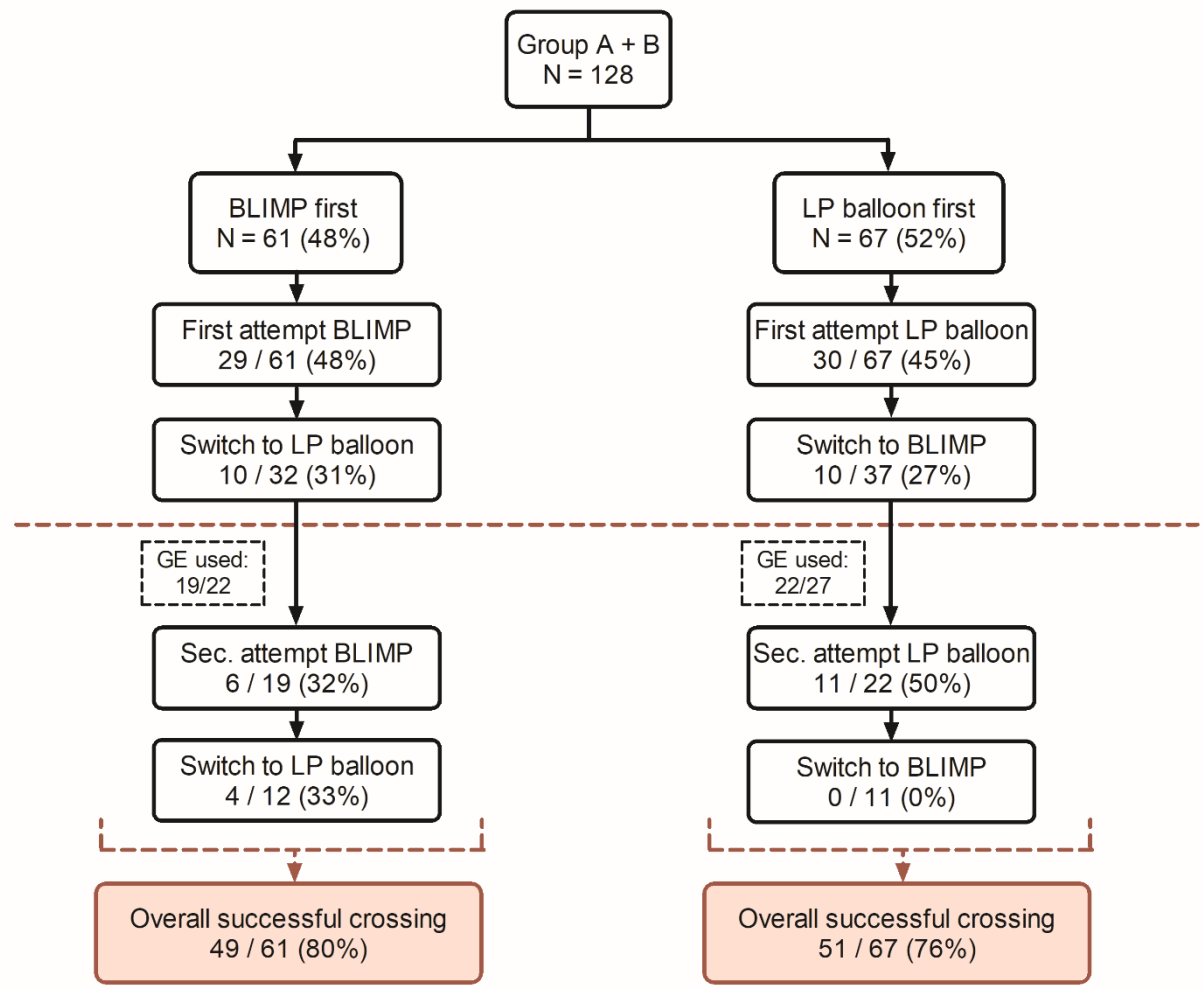

FIGURE 2 Enrollment and stepwise approach for successful crossing. LP= Low-profile. GE: Guide extension catheter.