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A prospective, multi-center study of the chocolate balloon in femoropopliteal peripheral artery disease: The Chocolate BAR registry

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Abstract

The Chocolate BAR study is a prospective multicenter post-market registry designed to evaluate the safety and performance of the Chocolate percutaneous transluminal angioplasty balloon catheter in a broad population with symptomatic peripheral arterial disease. The primary endpoint is acute procedural success (defined as ≤30% residual stenosis without flow-limiting dissection); secondary long-term outcomes include freedom from target lesion revascularization (TLR), major unplanned amputation, survival, and patency. A total of 262 patients (290 femoropopliteal lesions) were enrolled at 30 US centers between 2012 and 2014. The primary endpoint of procedure success was achieved in 85.1% of cases, and freedom from stenting occurred in 93.1%. Bail out stenting by independent adjudication occurred in 1.6% of cases and there were no flow limiting dissections. There was mean improvement of 2.1 Rutherford classes (±1.5) at 12-months, with 78.5% freedom from TLR, 97.2% freedom from major amputation, and 93.3% freedom from all-cause mortality. Core Lab adjudicated patency was 64.1% at 12 months. Use of the Chocolate balloon in an "all-comers" population achieved excellent procedural outcomes with low dissection rates and bailout stent use.

KEYWORDS

endovascular intervention, femoropopliteal peripheral artery, infrapopliteal peripheral artery, percutaneous transluminal angioplasty

1 | INTRODUCTION

Peripheral arterial disease (PAD) carries a significant global health burden, and can limit functional capacity and quality of life [1]. Percutaneous transluminal angioplasty (PTA) for PAD is often associated with suboptimal outcomes due to complications following balloon inflation related to vessel trauma and flow limiting dissections that may require bailout stenting. Novel strategies and techniques to enhance both acute and longer-term outcomes with PTA are needed.

The Chocolate PTA balloon catheter (TriReme Medical LLC, Pleasanton, CA) is a standard balloon constrained by a nitinol scaffold that sub-segments the balloon when inflated, creating valleys and grooves on the balloon surface that increase the contact surface area of the Chocolate balloon catheter (Figure 1). The intent of this balloon design is to disperse the force associated with angioplasty along this increased contact surface resulting in a controlled and differential dilatation approach to minimize overall vessel trauma. The Chocolate BAR post-market registry is intended to evaluate the safety and performance of the Chocolate PTA balloon catheter in a broad population.

FIGURE 1 The Chocolate balloon. The nitinol scaffold subsegments the balloon when inflated

2 | MATERIALS AND METHODS

This is a prospective multicenter post-approval study evaluating the use of the Chocolate PTA balloon in patients with femoropopliteal atherosclerotic disease at 30 US clinical centers. Patients with femoropopliteal disease were eligible for enrollment after successfully crossing the target lesions, if they had angiographic evidence of distal run-off immediately prior to the use of Chocolate Balloon and at least one patent tibial vessel. Patients were excluded if primary stenting was planned, if a flow-limiting dissection was present prior to Chocolate Balloon use, if life expectancy was <12 months or the patient was enrolled in another investigational study. The Institutional review board or ethics committee approved the trial and all patients provided informed consent. The cohort is defined by treatment of femoropopliteal vessel disease including the superficial femoral artery (SFA) and P1/P2 segments of the popliteal artery.

The Chocolate PTA Balloon is available in diameters of 2.0–6.0 mm and lengths of 20–120 mm. The Chocolate Balloon was sized 1:1 with the target vessel diameter. Multiple inflations and sizing up with a larger Chocolate Balloon in cases with residual stenosis were permitted with a recommendation to inflate the Chocolate balloon to half nominal for 30 sec followed by a slow inflation to nominal for an additional 90 sec. Prolonged balloon inflation with Chocolate or conventional PTA for at least 5 min was recommended for suboptimal results, and if no improvement, bail-out stenting was permitted.

Clinical evaluation and outcomes are reported up to 12 months. Clinical assessments were performed at 1, 6, and 12 months and included Ankle Brachial Index (ABI), Rutherford Assessments, and Duplex Ultrasound at each visit.

The primary endpoint was procedure success defined as a target lesion residual stenosis of ≤30% stenosis without a flow-limiting dissection after Chocolate balloon adjudicated by independent angiographic core laboratory analysis. Secondary study endpoints included the rate of acute bailout stenting for suboptimal results; improvement in Rutherford classification or ankle/toe brachial index from baseline; freedom from target lesion revascularization (TLR) at 1, 6, and 12 months; major amputation, defined as unplanned amputation at or above the ankle at 12 months; 6- and 12-month patency, defined as freedom from restenosis at the target lesion (diameter stenosis >50% based on duplex ultrasound and peak systolic velocity (PSV) ratio <2.5) without the need of TLR.

An independent clinical event committee (Yale Cardiovascular Research Center, Yale University School of Medicine, New Haven, CT) adjudicated all clinical events with causal relationship to the Chocolate Balloon. An independent angiographic core laboratory (Yale Cardiovascular Research Center, Yale University School of Medicine, New Haven, CT) reviewed and analyzed all angiograms using validated Quantitative Vascular Angiography (QVA) software (MEDIS, Leiden, The Netherlands). Dissections were classified according to the NHLBI Dissection Classification System (1985), which defines flow-limiting dissections as Types E and F. An independent Duplex ultrasound core laboratory (VasCor, Massachusetts General Hospital) reviewed all duplex ultrasounds using standard methodology. Severe calcification was defined as calcific radiopacities noted on both sides of the arterial wall by angiography prior to contrast injection and extending more than 1 cm of length.

TABLE 1 Baseline patient characteristics

	n = 262
Age, years mean (±SD)	69.7 ±10
Male gender	160 (61.1%)
Diabetes mellitus	132 (50.4%)
Hypertension requiring medications	241 (92.0%)
Hyperlipidemia requiring medications	222 (84.7%)
Obesity	42 (16.0%)
Prior stroke	24 (9.2%)
Prior MI	36 (13.7%)
History of CAD	151 (57.3%)
Current smoker	77 (29.4%)
Past smoker	151 (57.6%)
Baseline mean Rutherford Class, mean (SD)	3.3 ±1
0—Asymptomatic	0%
1—Mild claudication	1 (0.4%)
2—Moderate claudication	55 (21.0%)
3—Severe claudication	122 (46.6%)
4—Ischemic rest pain	34 (13.0%)
5—Minor tissue loss	50 (19.1%)
6—Major tissue loss	0%

MI, myocardial infarction; CAD, coronary artery disease.

3 | RESULTS

A total of 262 patients were enrolled over 30 months from June 2012 to December 2014. The 262 patients had 290 femoropopliteal atherosclerotic lesions enrolled at 30 sites in the United States. There was adequate data on 263 lesions for lesion analysis. At 12 months 203 (77.5%) patients completed follow-up or met the study endpoint and 12.6% withdrew consent. Another 9.9% were lost to follow-up.

Baseline characteristics are summarized in Table 1. Initial presentation with critical limb ischemia (CLI) occurred in 32.1%. The Chocolate PTA balloon was effectively delivered to and inflated at the intended lesion in 100% of cases (Table 2).

TABLE 2 Baseline and procedural lesion characteristics

Lesion characteristics	N = 263
Lesion length (mm)	83.5 ± 59.9 (*n* = 250)
Total occlusions	60/260 (23.1%)
Lesion calcification	
None/Mild	93/254 (36.6%)
Moderate	110/254 (43.3%)
Severe	51/254 (20.1%)
% diameter stenosis, pre-treatment (mean ± SD)	73.5 ± 17.3
% diameter stenosis, post-treatment (mean ± SD)	22.0 ± 8.4
Minimal lumen diameter (mm), pre-treatment (mean ± SD)	1.3 ± 0.9
Minimal lumen diameter (mm), post-treatment (mean ± SD)	4.1 ± 0.7
Acute luminal gain (mm) (mean ± SD)	2.8 ± 0.7
Achieved <=30% DS without flow-limiting dissection	85.1%

The primary endpoint (procedure success: ≤30% DS without a flow-limiting dissection) was achieved in 85.1% of patients with the Chocolate balloon (Table 2). Bail out stenting for a residual stenosis of >30% was used in 1.6% (*n* = 4). Dissections were identified in 22.5%; 2% grade A, 9.5% grade B, 10.7% grade C, 0.4% grade D; none were flow-limiting (grades E or F) by angiographic Core Laboratory. The 12-month patency (PSV ratio < 2.5 by duplex ultrasound and no TLR) was 64.1% by core lab and 68.3% by site report. At 12 months, freedom from TLR was 78.5% (Figure 2), freedom from major unplanned amputation 96%, and freedom from all-cause mortality 94%. Twelve-month clinical improvement was 89.3% with a 2.1 ±1.5 average decrease in Rutherford score.

Amongst the subgroup of patients with site-determined severe calcification (*n* = 77, 29.4%), freedom from TLR was 87% at 12-months. Freedom from TLR, absence of occlusion and PSV < 2.5 in the severely calcified group was 48.5%, with a 12-month primary patency of 72.7%, and freedom from amputation was 96%.

4 | DISCUSSION

The Chocolate Balloon Registry confirms, in a post market study, that the novel design of the Chocolate balloon is associated with excellent acute procedural results without flow-limiting dissections. This strategy affords the benefit of minimizing the use of bail out stenting and provides an alternative to primary stenting with excellent 12-month primary patency rates and low rates of TLR.

Endovascular techniques and outcomes with standard PTA and stenting have improved over time and have become first-line revascularization strategies for patients with symptomatic PAD. However with stenting, restenosis in the superficial femoral and/or popliteal artery continue to occur in 20%–50% of patients at 12 months [2–4].

Several biomechanical forces acting on the SFA during movement are inherent limitations that metallic stents cannot overcome. With leg movement, flexion points as well as muscular forces lead to ongoing compression, torsion, elongation and flexion forces that contribute to stent fracture, restenosis, and possibly in-stent thrombosis [5–7].

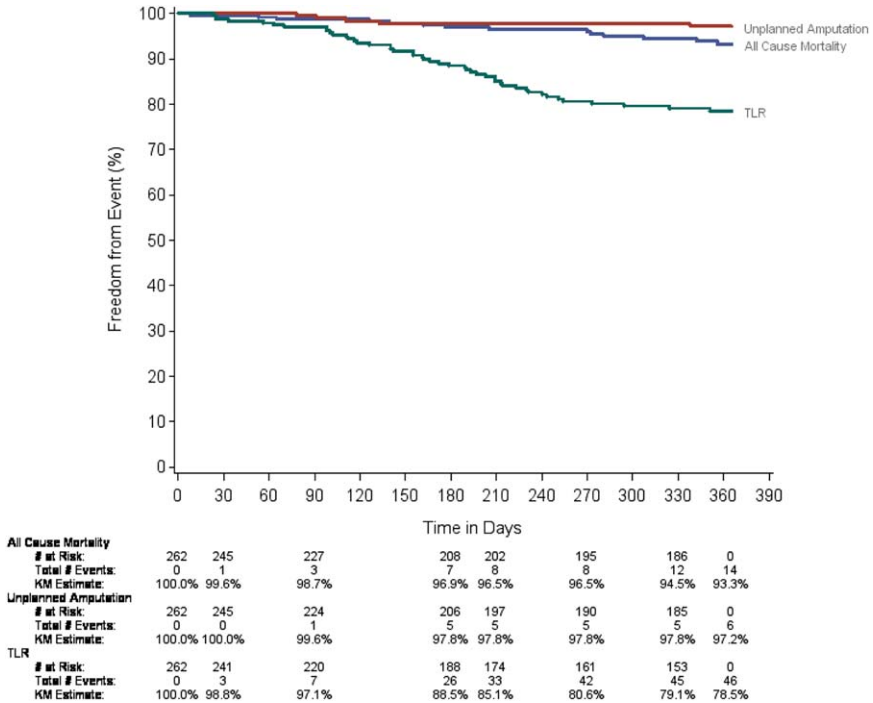

FIGURE 2 Kaplan–Meier—freedom from TLR, major unplanned amputation, all-cause mortality. [Color figure can be viewed at wileyonlinelibrary.com]

Self-expanding memory alloy stents, such as nitinol, intended to reduce stent fracture have not eliminated the problem with reported fracture rates at 1 year ranging from 2% to 18% in longer stented segments [8–11] and as high as 27% with overlapping stents [12]. An additional major challenge with stenting is diffuse in-stent restenosis or in-stent occlusion, which can be a very difficult problem to treat [2,13] with recurrent restenosis rates in excess of 70% at 1–2 years, though recent results have suggested improved outcomes with peripheral drug-eluting stents and DCB [14–16].

Given the limitations of stent implantation, a primary revascularization approach with the Chocolate balloon offers a viable therapeutic alternative to primary stenting that does not limit future treatment options; a major consideration given the chronic and progressive nature of PAD. The Chocolate BAR registry represents an "all comers" patient population, allowing high-risk Rutherford 5 and 6 patients, one-third presenting with CLI, as well as patients with severely calcified lesions and chronic total occlusions. The acute and long-term outcomes of the Chocolate balloon for femoropopliteal intervention are favorable compared to other non-sent approach in other high risk cohorts, with greater freedom from amputation and similar revascularization rates with the Chocolate balloon. For example, the all comers XLPAD Registry treated with non-stent interventions (42.6% atherectomy) reported a 15% repeat revascularization and 9.2% amputation rate [17]. Compared to standard PTA series, where reported primary patency are 52% with similar clinically driven TVR rates, an important advantage of the Chocolate Balloon is the absence of flow limiting dissections compared to those reported with standard PTA (60%–70%) [18]. Sirignano et al. [19] evaluated the Chocolate Balloon in 84 consecutive patients with Rutherford 3 claudication and femoropopliteal disease, in a single center study. After Chocolate Balloon angioplasty, drug-coated balloon angioplasty was utilized. At a mean follow-up of 12.3 months, freedom from TLR was 97.6% and Rutherford score improvement of 2 or more were seen in 85.4%. The extent of calcification did not appear to affect outcomes in this small study. In the recent Levant 2 trial, standard balloon angioplasty demonstrated a 1-year patency of 52.6%, clinically driven TVR of 18% but SFA dissection rates were 72.3% [20]. In comparison, the Chocolate balloon demonstrated a superior 12-month primary patency (64.1%) with dissection rates of only 22.5% and no flow limiting dissections.

The paclitaxel-coated Chocolate balloon (Chocolate Touch) received European CE Mark approval in 2015 and is currently being evaluated for safety and efficacy in the ongoing US IDE ENDURE trial. Preliminary data support the benefit of the combination of the low dissection and drug delivery single device option [21].

This study has limitations as a non-randomized "all-comers" registry with a broad range of indications and lesion locations. A third of the study population had CLI. We cannot report this cohort to represent all populations with PAD, however, as patients without one patent tibial artery were excluded. Furthermore, even though long lesions were treated, the mean lesion length was 83.5 ± 59.9 mm. The operator may have had an implicit bias against treating longer lesions with the Chocolate balloon alone. This study, however, is more representative and relevant to everyday clinical practice including patients with longer lesions, chronic occlusions, CLI, and heavy calcification. Also there was attrition, with loss to follow-up of 9.9% and study withdrawal of 12.6%, with 77.5% completing follow-up or meeting the study endpoint at 12 months.

5 | CONCLUSION

The Chocolate BAR Registry confirms that the "low trauma" mechanism of the Chocolate balloon achieved excellent procedural outcomes, low rates of dissection, and minimal bail out stent use with high long-term patency and low rates of revascularization despite the high complexity of the population. These data support the use of the Chocolate balloon for use in femoropopliteal lesions.

CONFLICT OF INTEREST

Nothing to report.

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