

Very high pressure dilatation for undilatable coronary lesions: indications and results with a new dedicated balloon

Gioel Gabrio Secco^{1,2,3}, MD; Matteo Ghione¹, MD; Alessio Mattesini¹, MD; Gianni Dall'Ara¹, MD; Liviu Ghilencea¹, MD; Kadriye Kilickesmez¹, MD; Giuseppe De Luca², MD, PhD; Rossella Fattori⁴, MD, PhD; Rosario Parisi⁴, MD; Paolo Nicola Marino², MD; Alessandro Lupi³, MD; Nicolas Foin¹, MsC; Carlo Di Mario^{1*}, MD, PhD, FESC, FACC, FRCP, FSCAI

1. NIHR Biomedical Research Unit, Royal Brompton & Harefield NHS Foundation Trust, London, United Kingdom; 2. Department of Clinical and Experimental Medicine, University of Eastern Piedmont, Novara, Italy; 3. Department of Interventional Cardiology, "Maggiore della Carità" Hospital, Novara, Italy; 4. San Salvatore Hospital, Pesaro, Italy

KEYWORDS

- calcific lesions
- coronary angioplasty
- drug-eluting stents
- non-compliant balloon
- percutaneous coronary intervention

Abstract

Aims: Calcific coronary lesions impose a rigid obstacle to optimal balloon and stent expansion and the 20 to 30 atm limit that non-compliant (NC) balloons reach can be insufficient. The aim of our study was to evaluate the safety and efficacy of a new dedicated super high pressure NC balloon (OPN NC[®]; SIS Medical AG, Winterthur, Switzerland).

Methods and results: We retrospectively evaluated a consecutive series of 91 lesions in which conventional NC balloons at maximal pressure failed to achieve an adequate post-dilatation luminal gain and were therefore treated with an OPN NC balloon up to 40 atm. Angiographic success was defined as residual angiographic diameter stenosis <30%. MLD and %DS were measured at baseline, after NC balloon, OPN NC balloon and stent implantation. Angiographic success was achieved in 84 lesions (92.3%). All of the remaining lesions received rotational atherectomy with the exception of two cases in which rotational atherectomy was not attempted because of small vessel size and excessive tortuosity. MLD and acute gain were significantly greater and % DS was significantly lower post OPN NC balloon compared with conventional NC balloon inflation ($p<0.001$). No coronary perforations occurred. No acute or 30-day follow-up MACE was reported.

Conclusions: When conventional NC balloons fail, the new OPN NC dedicated high pressure balloon provides an effective and safe alternative strategy for the dilatation of resistant coronary lesions.

*Corresponding author: Royal Brompton Hospital, Sydney Street, London, SW3 6NP, United Kingdom.
E-mail: c.dimario@rbht.nhs.uk

Abbreviations

54	ACT	activating clotting time
55	ATM	atmosphere
56	CABG	coronary artery bypass graft
57	CB	cutting balloon
58	DES	drug-eluting stent
59	DS	diameter stenosis
60	ISR	in-stent restenosis
61	IVUS	intravascular ultrasound
62	LVEF	left ventricular ejection fraction
63	MACE	major adverse cardiovascular events
64	MLD	minimum lumen diameter
65	MVD	multivessel disease
66	NC	non-compliant
67	OCT	optical coherence tomography
68	PCI	percutaneous coronary intervention
69	PTCA	percutaneous transluminal coronary angioplasty
70	QCA	quantitative coronary angiography
71	TIMI	thrombolysis in myocardial infarction
72	TVR	target vessel revascularisation
73	ZES	zotarolimus-eluting stent

Background

Heavily resistant coronary lesions remain a challenge in interventional cardiology. Calcification or dense fibrosis of the vessel wall or thick neointimal hyperplasia can create a rigid obstacle to uniform balloon expansion and optimal stent deployment that might result in an increased risk of in-stent restenosis (ISR) and stent thrombosis¹.

Increasing the pressure beyond the recommended limits during dilatation of resistant lesions often accentuates non-uniform balloon expansion with the consequent overdilatation of the more compliant segments at the lesion edges (so-called “dog-boning” effect) leading to an increased risk of vessel damage²⁻⁴.

Conventional non-compliant (NC) balloons have more predictable responses and more uniform dilatation than semi-compliant balloons, but even at pressures of 24-30 atm dog-boning also occurs.

A variety of devices and technologies have been developed to overcome these limitations. Cutting balloons (CB), designed to concentrate the dilatation force along three or four blades, are often too bulky to cross truly undilatable lesions and they also may fail to expand at their maximal pressures. Above 16 atm the risk of rupture is quite high, and a ruptured CB might become difficult to reinsert into the guiding catheter. Scoring balloons have a lower profile and accept higher pressure but their efficacy is limited⁵⁻⁹. Modification of the vessel wall compliance using rotational atherectomy is certainly the best option, but this technique requires specific expertise in handling a poorly steerable, uncoated 0.010 inch wire and advancing the burr. Excimer laser therapy has been described as an effective last resource in anecdotal cases but a laser is rarely available and perforations are possible. The complexity and the cost of these devices, together with the increased risk of coronary perforation, have hindered their widespread use¹⁰.

This registry tested the safety and efficacy of a dedicated, super high pressure non-compliant balloon (OPN NC®; SIS Medical AG, Winterthur, Switzerland) in a consecutive series of highly resistant coronary lesions.

Methods

LESION SELECTION

We evaluated 91 consecutive highly resistant coronary lesions in which conventional NC balloons failed to achieve an adequate post-dilatation luminal gain. After the failed attempt with the conventional NC balloon, the OPN NC balloon was inflated up to 40 atm (**Figure 1**). Other coronary lesions could be treated, when necessary. No exclusion criteria were applied. The OPN balloon is a CE

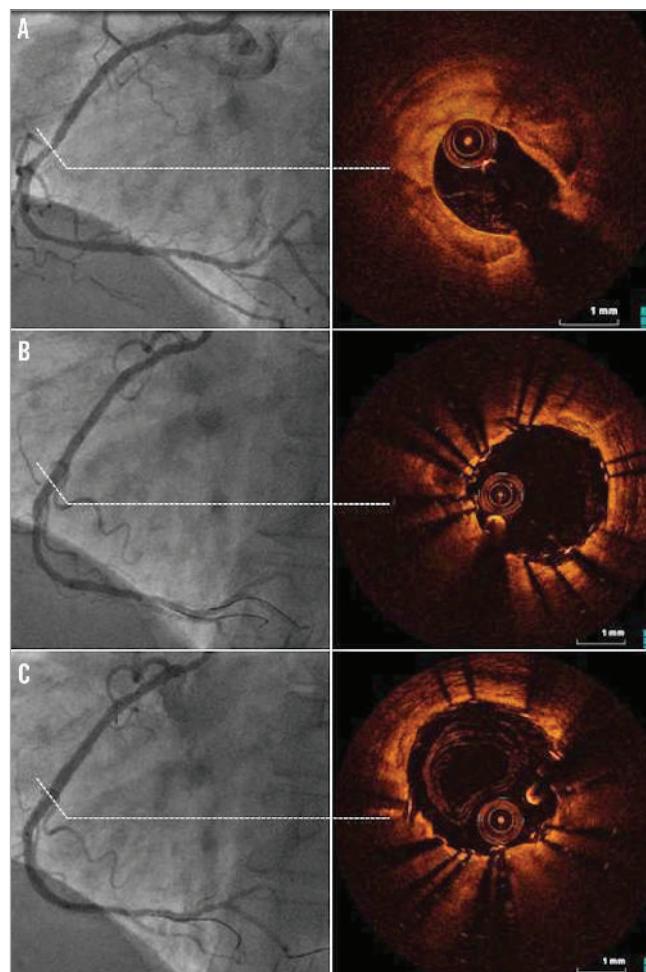


Figure 1. Angiographic and OCT images of a heavily calcified lesion pre-stenting (A), post 3.0×18 mm ZES implantation followed by an NC balloon inflated at 22 atm (B), and post-dilatation with a 3.0×15 mm OPN NC balloon inflated at 38 atm (C). Please note that the MLD increased to 2.92 mm (after the NC balloon dilatation) and to 3.18 mm (after the OPN NC dilatation). In the IVUS/OCT-guided PCI of the calcified lesion, we found calcium around the vessel contour accounting for at least >65% of the plaque, while OCT/IVUS imaging post-OPN NC dilatation shows diffuse vascular injuries following high pressure inflation but without a significant difference from the conventional NC balloon-treated lesions.

mark device. Patients signed informed consent for data treatment for scientific purposes, and the study was conducted according to the Declaration of Helsinki.

THE OPN NC BALLOON DEVICE

The OPN NC super high pressure balloon (SIS Medical AG) is a rapid-exchange percutaneous transluminal coronary angioplasty (PTCA) catheter compatible with 0.014" coronary wires. The most distinctive feature of the OPN NC balloon is the presence of proprietary twin-layer balloon technology, which permits the use of very high pressure inflations and ensures uniform expansion over a wide range of pressures (Figure 2). The balloon is highly non-compliant with a nominal pressure of 10 atm and a rated burst pressure of 35 atm (Table 1). Each balloon is factory tested at 45 atm. The balloon diameters currently available cover a range from 1.5 mm up to 4.0 mm with $\frac{1}{2}$ mm intervals. Lengths are 10, 15 and 20 mm. The commercial name OPN comes from an abbreviation of op(e)n.

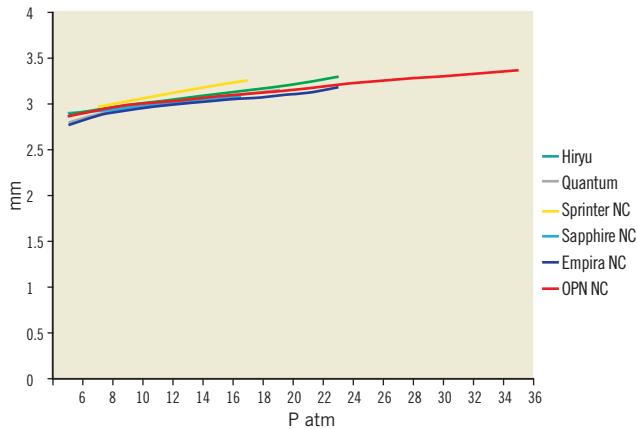


Figure 2. Comparison between different NC balloons compliance 3.0 mm diameter: Hiryu™ (Terumo Medical, Tokyo, Japan), NC Quantum Apex™ (Boston Scientific, Marlborough, MA, USA), NC Sprinter® RX (Medtronic, Minneapolis, MN, USA), Sapphire NCTM (OrbusNeich, Wanchai, Hong Kong, China), Empira™ NC (Cordis, Johnson & Johnson, Warren, NJ, USA), OPN NC® (SIS Medical AG, Winterthur, Switzerland). Please note that the OPN NC balloon is the only commercially available NC PTCA balloon catheter with a satisfactory compliance up to 35 ATM.

Table 1. OPN balloon compliance chart.

PRESSURE (ATM)	OPN NC 2.0	OPN NC 2.5	OPN NC 3.0	OPN NC 3.5	OPN NC 4.0
10	2.0	2.5	3.0	3.5	4.0
20	2.1	2.6	3.14	3.67	4.19
30	2.18	2.7	3.29	3.85	4.37
35	2.2	2.77	3.36	3.91	4.41

INTERVENTIONAL PROCEDURE

PCI was routinely performed with standard techniques via the femoral or radial approach using 6 or 7 Fr guiding catheters. Patients

not preloaded with oral aspirin and/or clopidogrel received a loading dose of intravenous aspirin (500 mg) and clopidogrel (600 mg) or prasugrel (60 mg) as standard practice in our catheterisation laboratory. Intravenous heparin (70 UI/Kg body weight) was administered before the procedure with subsequent boluses aimed at achieving an activated clotting time (ACT) of between 250 and 300 sec. The use of GP IIb/IIIa inhibitors was minimised and left to the discretion of the operator. In all cases, lesion predilatation was performed with a low-profile normal balloon slightly undersized according to conventional angiographic criteria. In case of incomplete balloon expansion with visible indentation at inflation pressures close to the rated burst pressure the lesion was approached using a conventional NC balloon inflated at least at the rated burst pressure and often higher. If this step also failed to provide an adequate luminal gain because of residual underexpansion of the balloon, the OPN NC balloon (with the same diameter as the NC balloon) was inflated up to 40 atm. Finally, all lesions were treated with DES optimised by NC balloon inflation when needed. In case of stent underexpansion with residual stenosis >40% assessed by angiography, the OPN NC balloon (with the same diameter as the NC balloon used) was inflated up to 40 atm for stent optimisation.

ANGIOGRAPHIC ANALYSIS

As is routine in our centre, standard image acquisition of the treated stenosis was performed using two or more angiographic projections after intracoronary nitroglycerine 100-200 mcg or isosorbide dinitrate 2-3 mg to provide maximum coronary dilation. We identified the projection where the lesion was best visualised and appeared more severe with no overlapping and minimal foreshortening. We filmed the lesion in this view during all balloon inflations and for final angiography. Quantitative coronary angiography (QCA) was performed using a computer-based QCA system (MEDIS, Leiden, The Netherlands) with the dye-filled guiding catheter used for calibration. MLD and %DS were measured at baseline, after conventional NC balloon dilatation, and after OPN NC balloon dilatation. The interpolated reference diameter was considered as reference segment diameter. Lesion length was defined as the distance from the proximal to the distal shoulder of the lesion. Acute gain after conventional NC balloon was defined as MLD (mm) post NC conventional balloon – baseline MLD (mm). Acute gain after OPN NC balloon was defined as MLD post OPN NC balloon (mm) – baseline MLD (mm). Incremental gain after OPN NC balloon was defined as MLD post NC OPN balloon (mm) – MLD post conventional NC balloon (mm).

FOLLOW-UP

Clinical events were evaluated post-procedure, during hospitalisation and at 30-day follow-up.

DEFINITIONS

Angiographic success was defined as the achievement of residual angiographic stenosis <30% assessed by visual estimation with TIMI 3 flow. Procedural success was defined as the achievement

of angiographic success without any MACE, defined as death, myocardial infarction and repeat revascularisation (coronary artery bypass graft [CABG] or percutaneous transluminal coronary angioplasty [PTCA]). Twelve-lead electrocardiograms were recorded before, immediately after the procedure and at hospital discharge. In-hospital MACE was defined as any MACE occurring during hospitalisation for the index procedure. Follow-up MACE was defined as myocardial infarction, death or target lesion revascularisation (any repeat PCI or CABG at the lesion site) occurring during the follow-up period. Postprocedural access site “bleeding” was defined according to TIMI criteria¹¹ and haematoma was defined as an arterial puncture site swelling >5 cm.

STATISTICAL ANALYSIS

Continuous variables were expressed as mean±standard deviation, while categorical variables were presented as numbers with percentage. Continuous variables were compared using the paired Student’s t-test. Categorical variables were compared using the chi-square test. A p-value <0.05 was considered statistically significant.

Results

Patients and lesion characteristics are shown in **Table 2** and **Table 3**, respectively. The average age was 69.4±9.5 years with a prevalence of male sex (80.2%) and standard distribution of risk factors (hypertension 82.4%, hypercholesterolaemia 69.2%, diabetes 46.1%, previous or current smoking 65.9%). Out of the 91 lesions, 54 were heavily calcified or fibrotic lesions (59.3%) in previously untreated vessels, and seven were ISR (7.7%) in which conventional NC balloons did not expand during predilatation. In the remaining 30 cases the OPN NC balloons were used after stent deployment for stent optimisation (33%). Procedural characteristics are shown in **Table 3**. Predilatation using a semi-compliant balloon was performed in all cases and was then followed by a successive

Table 2. Baseline patient characteristics.

Number of patients	91
Sex (male/female)	73/18 (80.2% 19.8%)
Age	69.4±9.5
Risk factors	
Hypertension	75 (82.4%)
Hypercholesterolaemia	63 (69.2%)
Smoking	60 (65.9%)
Family history	52 (57.1%)
Diabetes	42 (46.1%)
Prior MI	35 (38.4%)
Prior CABG	21 (23%)
Renal failure	19 (28.9%)
LVEF (%)	52.6±12.9
Clinical presentation	
Stable angina	76 (83.6%)
Unstable angina	11 (12%)
NSTEMI	4 (4.4%)
CABG: coronary artery bypass graft; LVEF: left ventricular ejection fraction; MI: myocardial infarction; NSTEMI: non-ST elevation myocardial infarction	

Table 3. Lesion and procedural characteristics.

Number of treated lesions	91
Vessel	
Left main	2 (2.2%)
LAD	45 (49.4%)
LCX	15 (16.5%)
RCA	26 (28.6%)
SVG	3 (3.3%)
Multivessel disease	43 (47.2%)
Lesion characteristics	
Length (mm)	21±12
True bifurcation	38 (41.7%)
Ostium involved	12 (13.2%)
Calcific lesion	37 (40.6%)
CTO	17 (18.7%)
Optimisation after stenting	30 (33%)
ISR	7 (7.7%)
Balloon	
Number of NC balloon/lesion	128/91 (1.4)
Final NC balloon inflation (atm)	21.4±2.8
NC balloon mean diameter	2.6±0.6
Number of OPN NC balloon/lesion	91/91 (1.0)
Final OPN NC balloon inflation (atm)	37.2±2.7
OPN NC balloon mean diameter	2.8±0.4
Number of stent/lesion	124 (1.35)
IVUS guided	21 (23.1%)
OCT guided	10 (11%)

CTO: chronic total occlusion; ISR: in-stent restenosis; IVUS: intravascular ultrasound; LAD: left anterior descending artery; LCX: left circumflex artery; NC: non-compliant; OCT: optical coherence tomography. RCA: right coronary artery; SVG: saphenous vein graft

dilatation using a conventional NC balloon, sized according to conventional angiographic criteria and inflated up to the rated burst pressure or slightly higher. A total of 128 NC balloons were used (1.4 per lesion). In all cases, the dilatation performed with the conventional NC balloon failed to achieve an adequate balloon expansion and luminal gain. After the failed attempt the OPN NC balloon with the same diameter as the conventional NC balloon was inflated up to 40 atm. A total of 91 OPN NC balloons were used (one per lesion). Angiographic success was achieved in 84 lesions (92.3%). In three severely calcified subocclusive stenoses (3.3%) the OPN NC balloon failed to cross, while in two cases, despite successful crossing, the OPN NC failed to achieve an adequate luminal gain (2.2%). All five lesions were finally successfully treated with rotational atherectomy (5.5%). The remaining two cases were undilatable lesions in small and tortuous vessels for which both rotational atherectomy and excimer laser therapy were deemed unsafe (2.2%). GpIIb/IIIa inhibitors were used in six patients (6.6%).

ANGIOGRAPHIC RESULTS

QCA analysis is shown in **Table 4**. Both MLD and acute gain were significantly greater and %DS was significantly lower post OPN NC balloon inflation compared with post plain NC balloon inflation (1.7±0.8 mm vs. 2.4±0.9 mm, p<0.001; 41.1±15.8%

Table 4. QCA analysis.

	Baseline	Post NC balloon	Post OPN NC balloon	p-value
RD (mm)	2.6±0.8	–	–	<0.001
MLD	0.7±0.3	1.7±0.8	2.4±0.9	
% DS	73.6±9.9	41.1±15.8	20.2±14.9	<0.001
Lesion length	11.9±6.4	–	–	
Acute gain (mm)	–	1.1±0.7	1.9±0.8	<0.001
Incremental gain (mm)	–	–	0.8±0.4	

DS: diameter stenosis; MLD: minimum lumen diameter; RD: reference diameter

vs. 20.2±14.9%, p<0.001). These results were achieved with no increase in balloon size but with a higher inflation pressure (37.2±2.7 atm vs. 21.4±2.8 atm, p<0.001) (Figure 3).

PROCEDURAL AND CLINICAL OUTCOME

Angiographic and technical success with OPN NC balloons was achieved in 84 lesions (92.3%). In the remaining seven cases (7.7%), five lesions were successfully treated with rotational atherectomy (5.5%), while the remaining two cases were undilatable lesions for which both rotational atherectomy and excimer laser therapy were not attempted because of small vessel size and excessive tortuosity (2.2%). No coronary perforation or balloon rupture and ST change were reported after the procedure. No in-hospital or 30-day MACE was reported. No major postprocedural bleeding was reported. Haematoma of the access site occurred in five patients treated by the transfemoral approach (5.5%).

dilatation. With the OPN NC balloon we were able to achieve a more than acceptable post-dilatation luminal gain in 92% of the cases without the need of additional expensive devices.

The mechanical properties of the arterial wall are critically dependent on the thickness, distribution and characteristics of the intimal plaque¹². Thick neointimal hyperplasia and severe coronary calcification contribute to increase the hoop stress to the point that even high pressure non-compliant balloons might be insufficient to overcome the hoop stress and induct a satisfactory dilatation.

During dilatation of resistant coronary lesions, the non-uniform balloon expansion with the consequent overexpansion of the more compliant segment (the so-called “dog-boning” effect) may lead to an increased risk of vessel wall damage, including edge dissections and coronary perforation. A variety of devices and strategies have been developed to overcome this limitation. Cutting balloons have been designed to relieve the vessel hoop stress by creating controlled small incisions in the vessel wall and they present the practical advantage that they do not move during inflation due to the stabilising effect of the blades. Cutting balloons present several advantages for the treatment of severe calcified lesions, allowing a larger luminal gain at lower pressure compared to balloon angioplasty alone and preventing late recoil due to the incisions created by the blades^{7,13}. The lack of clinical benefit observed in early studies of cutting balloon vs. conventional balloon angioplasty in *de novo* lesions has created scepticism on the potential mechanical usefulness offered by a focal concentration of force on the intimal plaque.

Mehran et al¹⁴ showed that when treating in-stent restenosis with balloon angioplasty, luminal gain is achieved by a combination of additional stent expansion and neointimal tissue compression through the stent, resulting in a displacement through the stent struts and compression of neointimal tissue. Although satisfactory initial clinical and angiographic results were obtained with balloon angioplasty, a significant early lumen loss was also observed shortly after in-stent restenosis treatment due to recoil and re-intrusion of neointimal tissue in the lumen¹⁵. This early phenomenon possibly influences the long-term outcome after balloon angioplasty for in-stent restenosis, affected by a high re-restenosis rate^{16,17}. Despite these findings, several randomised studies showed no real advantage of CB over PTCA with a conventional balloon and both the rigidity and the risk of balloon entrapment can limit their routine use during treatment of heavily calcified coronary lesions.

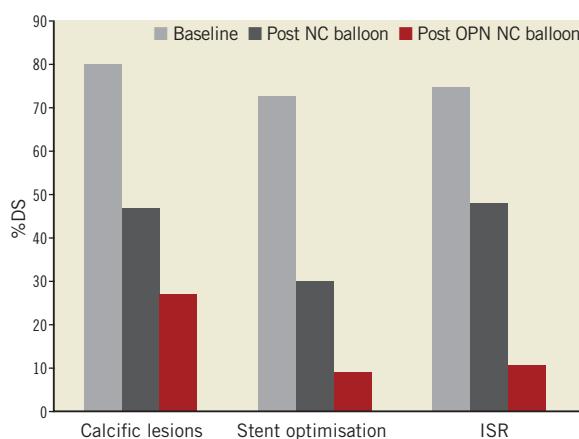


Figure 3. Decrease in % of diameter stenosis (DS) in calcific lesions (Group A), stent optimisation (Group B) and in-stent restenosis (ISR) (Group C). The incremental gain offered by the OPN NC balloon was sufficient to achieve angiographic success in all the three subgroups (0.81±0.47 mm in Group A; 0.77±0.41 mm in Group B; 1.34±0.31 mm in Group C).

Discussion

In our registry we tested the safety and efficacy of the OPN NC super high pressure balloon in a consecutive series of truly heavily resistant coronary stenosis nonresponsive to plain NC balloon

266 Modification of the vessel wall using rotational atherectomy and
 267 excimer laser therapy improves vessel wall compliance, thus facilitating
 268 uniform stent expansion.

269 Excimer laser therapy is based on the principle of photoablation,
 270 converting occlusive material into microbubbles which are immediately dissolved in the blood¹⁸. Its successful use during treatment
 271 of resistant coronary lesions has been described previously¹⁹.

272 Rotational atherectomy is a technique in which a small
 273 grinder is inserted into the coronary arteries to ablate the plaque.
 274 Specifically, it is effective in the treatment of calcified lesions
 275 because of its differential cutting mechanism, a phenomenon by
 276 which soft tissues (such as the normal arterial wall) are deflected
 277 so that the grinder will not contact them during high-speed rotation,
 278 while hard calcified plaques are not deflected and can be
 279 ablated by the grinder²⁰. Up-sizing the burr might enable better
 280 lesion modification, resulting in greater stent expansion and
 281 strut apposition. It is, however, unknown whether routine usage
 282 of aggressive rotational atherectomy is superior to conventional
 283 balloon dilatation as a means of lesion modification, followed
 284 by DES implantation, because of the lack of systemic long-term
 285 results of such a strategy^{21,22}.

286 Despite the fact that the majority of resistant coronary lesions can
 287 be treated with balloon dilatation and stent implantation alone²³,
 288 the rigid obstacle imposed by calcium or thick neointimal hyper-
 289 plasia might prevent an optimal balloon expansion and symmet-
 290 ric stent deployment, thus resulting in a gross malapposition of the
 291 stent struts. The importance of this is indirectly confirmed by find-
 292 ings from the e-Cypher registry correlating calcific lesions with
 293 the future occurrence of stent thrombosis²⁴. The real clinical con-
 294 sequence of strut malapposition is still matter of debate but surely
 295 it may impinge on the elution properties of DES, increase the acti-
 296 vation of fibrin and platelets, and thus result in accelerated inti-
 297 mal hyperplasia or stent thrombosis. Although the use of dedicated
 298 techniques such as rotational atherectomy might certainly improve
 299 procedural success in the treatment of resistant coronary lesions,
 300 the complexity, the cost and the need of dedicated operators have
 301 hindered their widespread application.

302 Conversely, the OPN NC super high pressure balloon is a plain
 303 rapid exchange PTCA catheter which can be attempted easily in case
 304 of the failure of conventional balloons²⁵. Thanks to its twin-layer
 305 technology, it allows the use of very high pressure inflations, ensur-
 306 ing uniform expansion over a wide range of pressures and reducing
 307 the risk of vessel damage²⁶. In our registry we found a significant
 308 increase of MLD and acute luminal gain after OPN NC balloon
 309 dilatation compared with plain NC balloon inflation. Moreover, as
 310 a consequence of the OPN NC's uniform expansion we had no ves-
 311 sel rupture despite the use of very high pressure inflations.

312 Limitations

313 The main limitation of the OPN NC balloon is its high profile
 314 which, together with the stiffness of the twin-layer technology, in
 315 the vast majority of cases undermines any attempt to recross when
 316 inflated. The balloon does not refold well, and after inflation it is

317 very difficult to use it again (for instance for both pre- and post-dil-
 318 ation). An independent core lab and multiple observer QCA anal-
 319 ysis would have improved reliability of data. Moreover, our results
 320 come from a small sample, retrospective and non-randomised com-
 321 parison which is certainly susceptible to selection bias.

Conclusions

When conventional NC balloons fail, OPN NC super high pres-
 322 sure balloons can provide an effective strategy for treatment of
 323 severely calcified coronary lesions. Moreover, our data suggest that
 324 the unique twin-layer technology offered by the OPN NC balloon
 325 achieves uniform balloon expansion, reducing balloon rupture, ves-
 326 sel damage and coronary perforation.

Impact on daily practice

Heavy calcified coronary artery lesions impose a rigid obstacle to optimal balloon expansion and symmetric stent deployment resulting in an increased risk of in stent restenosis and thrombosis. Surely, rotational atherectomy is the gold standard treatment for calcific lesions but its use in daily practice is limited by the cost and the need for dedicated operators. Conversely, the OPN NC high pressure balloon is a plain rapid exchange PTCA catheter which can be easily used in case of the failure of conventional balloons, providing a safe and easy alternative strategy in case of failure of conventional NC balloon dilatation.

Conflict of interest statement

The authors have no conflicts of interest to declare.

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