Coronary Stent Implantation Technique: Prolonged Inflation Time Maximizes Stent Expansion

Mrinal Saha, MD, Petra Poliacikova, MD, Adam de Belder, MD, Stephen Holmberg, MD, Michael Clarke, Ronak Rajani, MD, David Hildick-Smith, MD

ABSTRACT: Objectives. To determine whether longer periods of stent balloon inflation result in greater minimal luminal diameter (MLD) as measured by quantitative coronary analysis (QCA), and to determine whether measured size correlated with that predicted by pressure-diameter nomograms. **Methods.** Seventy-four stents were implanted in 52 patients. Stent acquisitions at a steady inflation pressure were taken at 10 s, 30 s, and 60 s. The stent MLD at each of these intervals was measured by QCA. Comparisons were made between (1) stent diameter obtained at these time intervals; and (2) nomogram-predicted pressure-related stent diameters. **Results.** Measured stent size increased significantly between each time point measured, with the most marked increment in size (0.15 ± 0.02 mm) observed between 10 s and 30 s (*P*<.0001), with a smaller but still significant increment between 30 s and 60 s (0.06 ± 0.02 mm; *P*=.0034). Although there was good correlation between measured size and expected size at 10 s and 30 s (r^2 = 0.60 and 0.58, respectively), the correlation at 60 s inflation was strongest (r^2 = 0.65). **Conclusions.** Longer durations of stent inflation increase MLD. A minimum duration of 30 seconds is recommended. However, even after 60 s, the MLD does not match the nomogram-derived expected diameter.

J INVASIVE CARDIOL 2013;25(1):28-31

Key words: stent balloon inflation, minimal luminal diameter

Incomplete apposition of stent struts due to under-expansion is associated with stent thrombosis using both bare-metal[1] and drug-eluting[2] stents. Stent under-expansion also appears to be associated with in-stent restenosis.[3] Intravascular ultrasound (IVUS) and optical coherence tomography (OCT) have been used to accurately determine the completeness of stent strut contact to the underlying arterial wall. However, cost and time considerations mean that these techniques are rarely used as a matter of routine. To avoid stent malapposition, operators attempt to select stent diameters to match vessel size using a combination of visual assessment, computer-calculated vessel size (quantitative coronary analysis: QCA), and comparison of vessel size with observed diameters achieved with predilatation balloons. Because of natural resistance to expansion of the atherosclerotic lesion, however, stents may not be expanded and opposed to the vessel wall throughout. Therefore, one strategy to deal with this phenomenon is expanding the stent further with another balloon inflation (postdilatation),[4] although this process adds time and expense. Ideally, therefore, the initial stent balloon inflation should be sufficient to achieve the ideal diameter of the reference vessel. Although stent manufacturers provide pressure-diameter nomograms, these values are obtained *in vitro*, so the final stent diameter achieved for a given inflation pressure may not correlate. One of the factors that may be responsible for this discrepancy between observed and predicted values is the length of time for which the stent balloon is inflated. There are limited data investigating the optimum time for which stents should be inflated, and as a consequence operators often inflate the stent balloon for a few seconds only. However, this period may vary depending upon both operator and lesion characteristics, and as a consequence the MLD achieved may be suboptimal.

The aims of this study were therefore: (1) to determine whether longer periods of stent balloon inflation result in greater stent diameter as measured by QCA; and (2) to determine whether measured size correlated with that predicted by pressure-diameter nomograms.

Methods

Patients undergoing elective or urgent angioplasty were recruited at our institution for a 3-month period during 2009. Inclusion criteria were: stable angina with failed medical therapy; or acute coronary syndromes requiring urgent coronary angiography. Exclusion criteria were: bifurcation lesions with side-branch ostial disease >70% or diameter >2.5 mm; acute ST-elevation myocardial infarction; pre-existing renal impairment (estimated glomerular filtration rate ≤90); and cardiogenic shock.

All patients received aspirin, clopidogrel, and weight-adjusted intravenous heparin. The procedure was performed by one of four experienced operators. After the injection of 500 µg intracoronary nitrate, angiograms were taken from at least 2 orthogonal projections at 25 frames/s, with the guide catheter adequately framed and free of contrast to allow accurate QCA analysis. The contrast agent iohexol (Omnipaque, GE Healthcare) was used for both

From the Sussex Cardiac Centre, Brighton and Sussex University Hospitals, United Kingdom.

Disclosure: The authors have completed and returned the ICMJE Form for Disclosure of Potential Conflicts of Interest. The authors report no conflicts of interest regarding the content herein.

Manuscript submitted May 16, 2012, provisional acceptance given June 19, 2012, final version accepted August 8, 2012.

Address for correspondence: Dr Petra Poliacikova, Brighton and Sussex University Hospitals NHS Trust, Sussex Cardiac Centre, Eastern Road, Brighton BN2 5BE, United Kingdom. Email: petra.poliacikova@bsuh.nhs.uk

Table 1. Stent dimensions and pressures.

Stent diameter (mm)	3.13 ± 0.41
Stent length (mm)	18.75 ± 5.34
Stent inflation pressure (atm)	16.84 ± 2.43
Predicted diameter (mm)	3.41 ± 0.43
MLD at 10 s (mm)	3.08 ± 0.60
MLD at 30 s (mm)	3.23 ± 0.61
MLD at 60 s (mm)	3.29 ± 0.62

MLD = minimal luminal diameter.

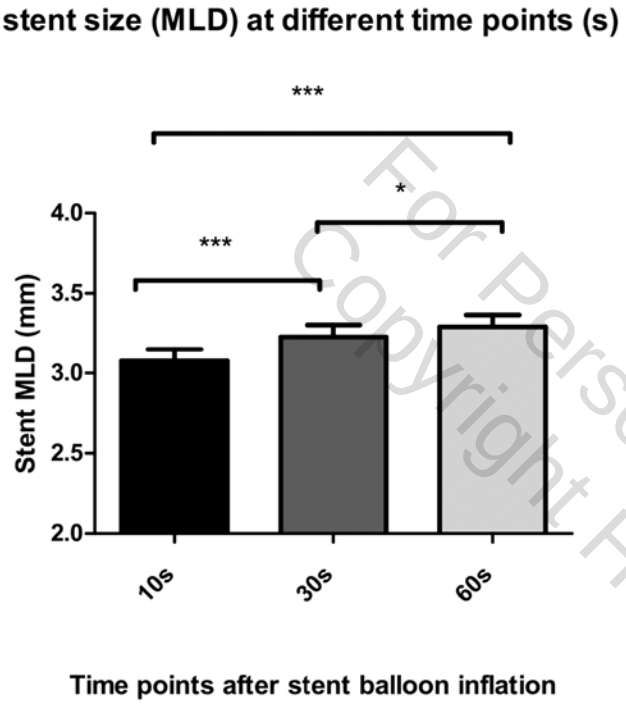


Figure 1. *Comparison of stent size (minimum luminal diameter) at different time points (10 s, 30 s, and 60 s).*

angiography and stent balloon preparation. Predilatation was performed in most of the cases, at the operator's discretion. Calcific lesions were routinely predilated, often with non-compliant balloons, in order to avoid eventual edge dissection after high-pressure deployment of stents mounted on more compliant balloons. Stent size was determined by visual inspection and by observed diameter achieved by predilatation balloons. Following appropriate positioning of the stent, the stent balloon was inflated rapidly (within 2 s) to the pressure of choice and maintained at this pressure. During stent balloon inflation, fluoroscopic acquisitions were taken at 10 s, 30 s, and 60 s intervals, after which the stent balloon was deflated. Following completion of the procedure, a senior radiographer blinded to the order of acquisition of images calculated the MLD of the stent at each of these time intervals with QCA (GE Centricity CA1000, GE Healthcare), using the guide catheter luminal diameter as a reference. Balloon inflation was ceased before 60 s in the presence of arrhythmias causing hemodynamic instability. All patients received adequate analgesia prior to commencing the procedure. Comparisons were made between: (1) stent diameters obtained at 10 s, 30 s, and 60 s time intervals; and (2) the nomogram-predicted value of stent diameter with that observed at each of the time intervals.

Statistical analysis. All values are given as mean ± standard deviation unless otherwise indicated. Comparison between stent diameters was made using a paired t-test or repeated measures one-way ANOVA when three or more groups were compared, in which case the Bonferroni correction was performed. All sample values conformed to a Gaussian distribution, as assessed by a Kolgmogorov-Smirnov test. $P<.05$ was considered significant. Prism version 5 (GraphPad Software, Inc) was used for all analyses.

Results

Fifty-two patients were recruited, with a mean age of 65.5 ± 11.8 years, and body mass index of 28.6 ± 5.2 kg/m^2. Seventy-four stents were implanted, of which 58 were drug-eluting stents, and 16 bare-metal stents. Drug-eluting stents included Biomatrix (n = 44), Cypher (n = 2), and Xience (n = 12). Bare-metal stents included Driver (n = 1), Liberte (n = 5), Prokinetic (n = 1), Titan (n = 8), and Vision (n = 1). Seven stents were implanted in ostial locations. Mild-to-moderate fluoroscopic calcification was evident in 24 stent implantations. The mean inflation pressure was 16.84 ± 2.43 atm.

Mean stent sizes at each time point are shown in Table 1. Measured stent size increased significantly between each time point, with the most marked difference observed between 10 s and 30 s ($P<.0001$) and between 10 s and 60 s inflation ($P<.0001$). The difference between 30 s and 60 s was also, however, significant ($P=.0034$) (Figure 1).

There was a significant difference between measured and expected stent diameters at 10 s ($P=.005$). The difference became less significant at 30 s ($P=.057$) and not significant after a 60 s inflation ($P=.21$).

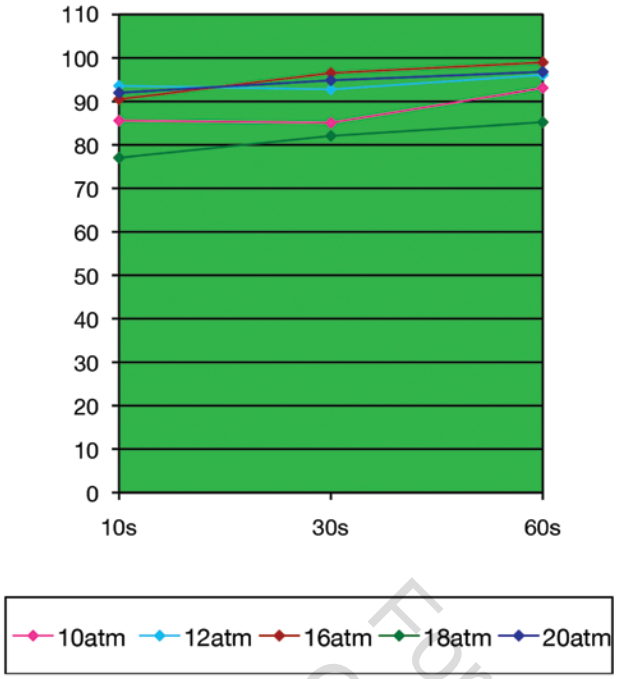
The correlation between measured size and expected size was the strongest at 60 s inflation ($r^2 = 0.65$) and weaker at 10 s and 30 s ($r^2 = 0.60$ and 0.58, respectively). If the group with fluoroscopic calcification was analyzed separately, these correlations surprisingly were noted to be stronger ($r^2 = 0.64$, 0.65, and 0.73 at 10 s, 30 s, and 60 s, respectively).

If lesions that received lower inflation pressures (10-14 atm) were analyzed separately (n = 9), strong correlations remained between expected and measured size ($r^2 = 0.69$, 0.69, and 0.73 at 10 s, 30 s, and 60 s, respectively).

No significant differences were observed if bare-metal stents were considered separately from drug-eluting stents.

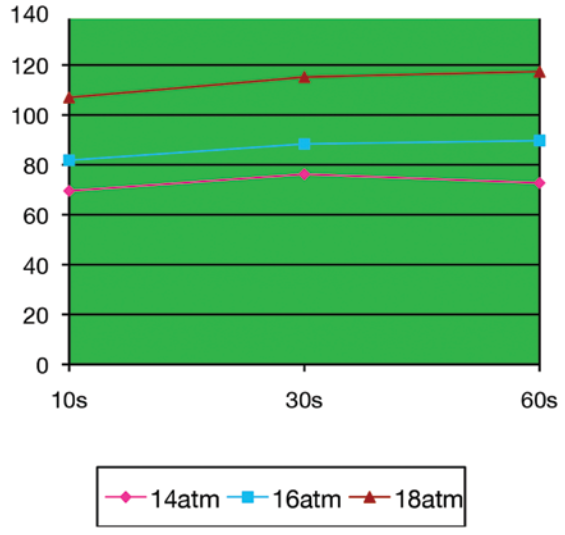
Discussion

Prolonged stent inflation appears to increase the diameter of the stent up to 60 s after initial balloon inflation, but even at 60 s does not match the expected diameter as measured by QCA.



Biomatrix	0h 0m 10s	0h 0m 30s	0h 1m 0s
10atm	85.58	85.08	93.11
12atm	93.59	92.76	96.10
16atm	90.51	96.55	99.00
18atm	77.04	82.08	85.22
20atm	92.00	94.85	96.82

Figure 2. *Biomatrix stent mounted on semi-compliant balloon. Relationship between the inflation pressure, inflation time, and final stent diameter expressed in percentage of nomogram-predicted diameter.*



Xience	0h 0m 10s	0h 0m 30s	0h 1m 0s
14atm	69.53	76.26	72.72
16atm	81.82	88.40	89.72
18atm	107.00	115.20	117.37

Figure 3. *Xience stent mounted on compliant balloon. Relationship between the inflation pressure, inflation time, and final stent diameter expressed in percentage of nomogram predicted diameter.*

The greatest increment in mean stent size occurred between 10 s and 30 s inflation (0.15 mm), compared to 30 s and 60 s (0.06 mm), which most likely reflects the tissue elastic properties of the vessel wall, given that the pressure was maintained at a constant level throughout 60 s.

Several lesion and stent characteristics may have impact on the final stent expansion. Unexpectedly, fluoroscopic evidence of calcification did not appear to interfere with the stent expansion in our study, which is perhaps a product of the small sample size, although better preparation of the calcific lesions with predilatation may have played a role.

Too few data were available to conclude whether ostial lesions or bare-metal versus drug-eluting stents might influence stent expansion over time.

The compliance of the stent delivery balloon clearly plays a role in the final stent expansion. The newer-generation stents used in our study, including Biomatrix, Titan, Driver, and Prokinetic, are mounted on semi-compliant balloons while the delivery balloons of Xience, Cypher, and Vision are made of compliant materials. Our study was not powered to show whether individual stent types were more prone to gradual increased expansion than others. However, for illustration, we constructed the pressure/time curves for our most frequently used compliant (Xience) and semi-compliant (Biomatrix) balloons (Figures 2 and 3). Both stent types increase their size with longer inflation times. Those mounted on compliant balloons expand faster (most of the expansion within the first 30 s) and the final diameter is more pressure dependent. While the increase in size is more gradual for stents with semi-compliant balloons, significant growth was still observed between 30-60 s (especially when lower inflation pressures were used).

Data are scarce with regard to the question of the ideal duration of stent balloon inflation. An early report investigated the impact of the duration of angioplasty balloon inflation alone upon vessel size, as measured with angioscopy.[5] Evidence suggested that longer inflation times, in this case ≥12 min compared to 3-5 min led to less immediate residual luminal stenosis.

More recently, a report has documented that longer inflation times (60 s vs 10 s) led to greater cross-sectional area of the artery as measured by IVUS.[6] However, the short vs long inflation times were carried out in different vessels, so it may be argued that observed differences may have been confounded by vessel characteristics rather than duration of balloon inflation.

Prolonged inflation time (60 s vs 20 s) was shown to result in larger MLD and stent expansion ratio (SER) in a study by Kawasaki et al that examined and compared the stent expansion of sirolimus- and paclitaxel-eluting stents.[7]

In both stent groups, the 60 s inflation resulted in approximately 80% SER as opposed to approximately 70% with the 20 s inflation. In our work, the stents reached

88.2 ± 11.5% of the nomogram-predicted diameter at 10 s and 95.3 ± 11.4% at 60 s; however, our work did not take into account the acute stent recoil, which is one of the denominators of the final stent diameter.[8,9]

The trend toward greater stent expansion was also found in a recent *in vitro* study using stainless-steel stents, where intrastent ultrasound measurements were used to try to determine the optimum time of stent balloon inflation.[10] The authors reported that the relationship between stent size and duration of inflation was exponential, and that optimum expansion was obtained at 30 s as opposed to 15 s, with only incremental increases in size obtained after 60 s or 90 s.

There are two ways in which this study may be of use in everyday clinical practice. First, the knowledge that longer inflation time increases stent expansion should encourage operators to use longer inflation duration as standard. Second, if on initial inflation a stent appears to the naked eye to be undersized, continuing inflation for a full 60 s will allow the stent to expand further, potentially achieving the correct visual diameter and obviating the need for postdilatation with its attendant risk of geographical miss.

Study limitations. Use of QCA may be relatively inaccurate compared to IVUS in determining stent expansion. However, the purpose of the study was to determine the validity of longer stent balloon expansion times in an everyday setting where IVUS or OCT are rarely used as a matter of routine.

Clearly, angiographic evidence of stent expansion does not necessarily equate to better longer-term follow-up, but this study was not designed to address this question. Clinical endpoint measurements would require larger numbers and more stringent evaluation of clinical risk factors.

Different stent types and stent platforms were used in this study; however, their specific characteristics were taken into account by manufacturers in the nomograms, and therefore should not confound our study.

The stent inflation pressures were left to the operator's discretion and varied throughout the study to a certain extent. The inflation pressure may have an impact on the rate of stent expansion: higher pressures may result in faster diameter growth and most of the expansion early during the inflation, while lower pressures may result in more gradual expansion requiring longer inflation times to achieve the target diameter. This was not taken into account in our study as we aimed to reflect real life, where inflation pressures vary significantly. Evaluation of relationship between inflation pressure, inflation time, and final diameter would require a substantially larger database.

There are insufficient data to make a comparison between the expansile characteristics of bare metal vs drug-eluting stents. In our practice, however, the use of DESs is proportionally greater than bare-metal stents in general, and this study again reflects the day-to-day clinical experience in this regard. In addition, immediate stent recoil following balloon deflation was not examined in this study, due to the limitations of assessing stent diameter without performing IVUS on all cases.

Conclusion

The current study addresses *in vivo* the question of the optimum duration of stent balloon inflation using QCA, measuring stent expansion in the same artery over time. At 60 s, there is evidence of increased stent diameter compared to 30 s, although most expansion has occurred by 30 s. Longer inflation times than are currently used in daily practice are to be recommended to optimize stent expansion.

References

1. Uren NG, Schwarzacher SP, Metz JA, et al. Predictors and outcomes of stent thrombosis: an intravascular ultrasound registry. *Eur Heart J.* 2002;23(2):124-132.
2. Fujii K, Carlier SG, Mintz GS, et al. Stent underexpansion and residual reference segment stenosis are related to stent thrombosis after sirolimus-eluting stent implantation: an intravascular ultrasound study. *J Am Coll Cardiol.* 2005;45(7):995-998.
3. Fujii K, Mintz GS, Kobayashi Y, et al. Contribution of stent underexpansion to recurrence after sirolimus-eluting stent implantation for in-stent restenosis. *Circulation.* 2004;109(9):1085-1088.
4. Romagnoli E, Sangiorgi GM, Cosgrave J, Guillet E, Colombo A. Drug-eluting stenting: the case for post-dilation. *JACC Cardiovasc Interv.* 2008;1(1):22-31.
5. Cribier A, Jolly N, Eltchaninoff H, et al. Angioscopic evaluation of prolonged vs standard balloon inflations during coronary angioplasty. A randomized study. *Eur Heart J.* 1995;16(7):930-936.
6. Asano T, Kobayashi Y, Fukushima K, et al. Effect of balloon inflation time on expansion of sirolimus-eluting stent. *Heart Vessels.* 2009;24(5):335-339.
7. Kawasaki T, Koga H, Serikawa T, et al. Impact of a prolonged delivery inflation time for optimal drug-eluting stent expansion. *Catheter Cardiovasc Interv.* 2009;73(2):205-211.
8. Aziz S, Morris JL, Perry RA, Stables RH. Stent expansion: a combination of delivery balloon underexpansion and acute stent recoil reduces predicted stent diameter irrespective of reference vessel size. *Heart.* 2007;93(12):1562-1566.
9. Carrozza JP Jr, Hosley SE, Cohen DJ, Baim DS. In vivo assessment of stent expansion and recoil in normal porcine coronary arteries. *Circulation.*1999;100(7):756-760.
10. Trindade IS, Sarmento-Leite R, Santos de FM, Gottschall CA. Determination of the minimum inflation time necessary for total stent expansion and apposition: an in vitro study. *J Invasive Cardiol.* 2008;20(8):396-398.