

Duration of dual antiplatelet therapy in elective drug coated balloon angioplasty

Natasha H Corballis^{1, 2}, MBBS, MRCP; Upul Wickramarachchi¹, MBBS, MRCP; Vassilios S Vassiliou^{1, 2 *}, MA, MBBS, PhD, FESC, FACC, FRCP Edin, Simon C Eccleshall¹, MBChB, MRCP, MD

¹ Department of Cardiology, Norfolk and Norwich University Hospital NHS Foundation Trust, Colney Lane, Norwich, UK, NR4 7LJ, UK

² Norwich Medical School, University of East Anglia, Bob Champion Research and Education, James Watson Road, NR4 7UQ, UK

*Corresponding author:

Dr Vassilios S Vassiliou
Norwich Medical School,
University of East Anglia
Norwich Research Park
Norwich NR4 7UQ
United Kingdom

Tel: 01603 592534

Email: v.vassiliou@uea.ac.uk

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- Coronary intervention

Abstract

Objectives:

We sought to answer whether one-month duration of dual antiplatelet therapy (DAPT) is safe after elective drug-coated balloon only (DCB) angioplasty.

Background:

The duration of DAPT after elective DCB was called into question after the ESC Focused DAPT Update of 2017. Until then, a one-month duration of DAPT was considered safe by national consensus groups (German, Italian and Chinese) supported by data from prospective worldwide registries.

The ESC Guidelines recommended a 6-month duration of DAPT based on evidence from in-stent restenosis randomized controlled trials only.

Methods:

Retrospective, real-world population, single-center analysis was conducted from January 1st, 2012 to March 31st, 2017 from a high-volume, tertiary PCI centre. All patients who received a one-month duration of DAPT after elective DCB angioplasty were included. We identified a primary composite outcome of cardiac death, myocardial infarction and target lesion revascularisation at 6-months.

Results:

This included 303 patients (78.5% male) with a mean age of 67±12.5. This incorporated 86.1% *de novo* lesions and 56.5% non-small (≥3mm diameter) coronary arteries treated. There were no reported outcomes of lesion thrombosis, target vessel MI, target lesion

revascularization or cardiac death at 6-months. There were two (0.6%) non-target vessel MIs and one (0.3%) non-cardiac death.

Conclusion:

One-month duration of DAPT appears safe after elective DCB-only angioplasty, highlighting this strategy for patients at high-risk of bleeding. These results also show favorable clinical outcomes for *de novo* coronary artery disease and non-small coronary arteries treated with DCB-only angioplasty. A one-month duration of DAPT appears a safe and attractive option.

Introduction

A lot of interest has been generated lately about the use and safety of DCB angioplasty focused mainly on peripheral intervention^{1,2,3,4}. However, the use of drug coated balloons (DCB) for coronary intervention has also been steadily increasing over the last few years and as more studies report encouraging results^{5,6}, DCB-only angioplasty for coronary disease is expected to increase further. Original recommendations for DCB use came from the German Consensus Group^{7,8} which also addressed the duration of dual antiplatelet therapy following DCB; stating that four weeks of dual antiplatelet therapy (DAPT) with aspirin and clopidogrel were deemed appropriate in patients with stable coronary disease with monotherapy life-long thereafter. The evidence for this came from small to moderate randomized controlled studies and large prospective worldwide registries. This was followed by the Italian Society of Interventional Cardiology⁹ and the Chinese Expert Group¹⁰, both supporting the German recommendation of one-month DAPT for stable coronary disease.

However, The European Society of Cardiology (ESC) Focused Update on DAPT 2017 took a different view and advocated a 6 month duration of DAPT in DCB angioplasty¹¹. This recommendation was supported by circumstantial evidence from three randomized control trials comparing DCB with drug eluting stents (DES) for in-stent restenosis only, whilst no DCB studies in *de novo* coronary intervention were included. In these three studies the duration of DAPT varied from 3 to 12 months.¹²⁻¹⁴ In RIBS-IV DAPT of a 3-month duration was given in the DCB arm, PEPCAD China ISR gave a 12-month duration of DAPT and ISAR-DESIRE-3 gave a 6-month minimum duration of DAPT. Of significance, is that bleeding events were not addressed in any of these three studies.

Following the publication of the ESC Focused Update 2017, there has been data from two important studies in *de novo* coronary disease. Firstly, the Basket-Small 2 was a randomized control trial comparing DCB with DES for small vessel *de novo* coronary disease and gave a one-month duration of DAPT to the DCB arm in all patients with stable coronary disease⁵. Secondly, Debut, a randomized trial comparing BMS to DCB in patients with high bleeding risk, also gave a one-month duration of DAPT for DCB angioplasty; thus suggesting that a full 6 month course of DAPT might not be necessarily required when a DCB-only approach is used.

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Although DCB angioplasty holds a class 1 recommendation by the ESC for in-stent restenosis angioplasty, there is now increasing evidence supporting the use of DCB for *de novo* coronary disease.⁵ As this use is projected to expand further we felt it was important to interrogate our existing DCB registry, a dedicated registry at the Norfolk and Norwich University Hospital including all patients who receive DCB-only angioplasty, to identify if a shorter one-month DAPT is safe in routine clinical practice. This is, to our knowledge, the first study using a real-world population to specifically answer the question regarding the safety of one-month DAPT in DCB-only angioplasty.

Materials and Methods

We retrospectively identified all patients from our local registry from January 1st, 2012 to 31st March 2017 who had undergone elective DCB-only angioplasty for stable coronary artery disease and received one-month DAPT. Institutional approval was obtained from Norfolk and Norwich University Hospital, UK and in line with other research of retrospective nature the need for patient consent was waived.

We included both *de novo* lesions and in-stent restenosis (ISR) lesions. Clinical outcomes were obtained through electronic clinical records and up-to-date mortality data was obtained from the Demographic Batch Service Bureau of the Health and Social Care Information Centre, a National database where all deaths are recorded. All patients who had a concomitant use of oral anticoagulant were excluded, as were those who underwent a staged procedure following acute coronary syndrome, with a pre-mandated 12-month duration of DAPT.

We defined a 6-month device-oriented primary composite end-point of cardiovascular death, myocardial infarction (not clearly attributed to a non-target vessel) and target lesion revascularization (clinically driven) in keeping with the ARC-2 recommendation for device outcome reporting.¹⁵ We chose the 6-month cutoff point following the ESC guidelines recommended cessation period for DAPT, as after this time monotherapy would have continued with the ESC guidelines also.

Myocardial infarction was defined as presence of chest pain or ischemic ECG changes with a rise in cardiac enzyme troponin and with no other vessel clearly identified as the culprit vessel.

Cardiac death was defined in accordance with the 2017 Consensus Report on Cardiovascular and Stroke Endpoint Definitions for Clinical Trials¹⁶ and included:

- 1) death resulting from an acute myocardial infarction (AMI),
- 2) sudden cardiac death,
- 3) death due to heart failure (HF),
- 4) death due to stroke,
- 5) death due to cardiovascular (CV) procedures, and
- 6) death due to CV hemorrhage.

Secondary outcomes included: non-cardiac death, lesion thrombosis and non-target vessel myocardial infarction.

Lesion thrombosis was defined as acute (<1 day), sub-acute (1 to 30 days), and late (>30 days) and defined in parallel to the ARC guidelines on Stent Thrombosis. ¹⁷

All procedural elements were at the discretion of the operators with practice based on guidelines for DCB angioplasty as previously reviewed. ¹⁸ All adverse events were independently adjudicated.

Results

Patient characteristics

A total of 303 patients were identified with 361 lesions treated with DCB-only PCI electively for coronary disease and who received DAPT for one month only. The cohort included mainly male patients (78.5%), with a mean age of 67±12.5 with 39.6% having had prior PCI, 9.6% having had prior CABG and other risk factors as outlined in table 1. These findings are in keeping with contemporaneous stable angina studies. ^{12, 13, 14}

Table 1: Patient Characteristics

Following one-month DAPT all patients continued with aspirin monotherapy thereafter. Some 96.4% received aspirin and clopidogrel for one month, 2.2% received aspirin and ticagrelor and 1.4% received aspirin and prasugrel. The use of ticagrelor or prasugrel was only due to previously documented intolerance to clopidogrel.

Lesion and procedural characteristics

Of 361 lesions treated, 86.1% were *de novo* lesions, the remaining 13.9% being in-stent restenosis lesions. The majority of lesions treated were left anterior descending artery (48.2%), 24.1% circumflex, 23% right coronary artery, 3.6% left main stem and 1.1% vein grafts. The DCBs used as follows: 143 (39.6%) were SeQuent Please (B Braun Melsungen AG, Germany), 186 (51.5%) were SeQuent Please NEO (B Braun Melsungen AG, Germany), 31 (8.6%) were IN.PACT Falcon (Medtronic, Inc., Santa Rosa, California, USA) and 1 (0.3%) were DIOR (Eurocor GmbH, Germany). Lesion complexity was assessed using The American College of Cardiology/ American Heart Association (ACC/AHA) Task Force on Assessment of Diagnostic and Therapeutic Cardiovascular Procedures classification system,¹⁹ and is summarized in Table 2.

Some 43.5% of lesions were small vessels (with DCB diameter of <3mm used) whilst 56.5% were large vessel with DCB diameter used was ≥ 3 mm.

Table 2: Lesion Characteristics

Clinical outcomes

Follow up at 6 months was 100% with patient outcomes shown in table 3. There were no reported occurrences of lesion thrombosis, target lesion MI or cardiac death at 6 months. There were no TLRs at 6-months. There was 1 (0.3%) death at 50 days due to end stage renal failure. There were 2 (0.6%) non-target vessel MIs, one at 49 days and one at 156 days. On both follow-up angiograms, the target lesion result was acceptable.

Table 3: Outcomes

Discussion

DCB angioplasty currently holds a class Ia recommendation for its use in ISR in accordance with the current ESC Guidelines¹¹, although there is increasing evidence to support its use for *de novo* coronary disease.^{5,4} With this use of DCB angioplasty predicted to increase, it is important to determine a safe duration for DAPT for elective procedures, a gap in the literature inadvertently highlighted by the ESC Focused Update on DAPT. Although recommending a 6-month duration of DAPT, the evidence studied to reach this decision was only from ISR RCTs and did not incorporate any *de novo* DCB literature, whilst previous Consensus Groups and National Societies had recommended a one-month duration of DAPT for DCB angioplasty in stable coronary disease. A recent literature search and sub-group analysis presented by Kleber *et al.*²⁰ reviewing all published RCTs and registries including *de novo* coronary disease suggested a one-month duration of dual antiplatelet therapy after DCB angioplasty was safe. This has been furthermore consolidated with recent RCTs which gave a one-month duration of DAPT for stable CAD.^{5,4}

We sought to answer whether a one-month duration of DAPT for stable coronary disease is safe. We conducted a retrospective analysis, using a real-world population, incorporating 361 lesions in 303 patients, of which 85.9% were *de novo* lesions. We found that one-month DAPT duration was safe with regards to lesion thrombosis, target lesion MI, TLR and cardiac death, with zero adverse outcomes at 6 months. This extends the evidence from current trials to include *de novo* coronary anatomy, and importantly, also incorporates data on non-small coronary vessels (as 56.5% in our cohort were $\geq 3\text{mm}$), which to this point was an evidence-free area. As such, our results are expanding on the previous work by Kleber *et al.*,²⁰ and the Basket-Small RCT⁵.

Of note, our clinical outcomes are reporting significantly lower rates of MACE than other real-life registry data.²¹ Several potential explanations for the difference in outcome include a shorter clinical end-point (6-month versus 9-month), smaller numbers, increased operator skill in a single-center doing a large volume of DCB only angioplasty and improved technique for DCB delivery. These improved clinical outcomes may be an indicator that due to improved technique and operator skill with DCB techniques, clinical outcomes with DCB only angioplasty are better than initially reported in registry data.

Acknowledging that bleeding rates after successful PCI are independently associated with a higher morbidity and mortality rate²² and a shorter duration of DAPT has been shown to be beneficial in risk reduction in those with higher bleeding risk in prospective registry studies^{23 24}, we believe that our data provides compelling evidence that can potentially extend the role of DCB angioplasty to those patients at high bleeding risk by enabling a shorter but safer one-month DAPT.

Limitations

Our study consists of only a small number of ISR lesions and subsequently our conclusions on that sub-group are less robust and a separate analysis with larger numbers may be warranted given the duration of DAPT in current RCT evidence ranges from 3-12 months.

In addition, selection bias and confounding errors are inherent limitations of a retrospective, single-center analysis. However, to limit this, we included all consecutive patients in our registry with a catchment area of over one million people. Furthermore, our patient demographics are similar to other contemporaneous DES studies in the UK^{12, 14, 13} indicating

that significant selection bias was unlikely. Finally, as we undertake more than 40% of our PCI with a DCB-only approach, we feel this would have minimized bias.

Conclusion

A one-month only duration of DAPT following elective DCB-only angioplasty appears safe, specifically for *de novo* coronary disease, in both small and non-small vessel disease and is the first report of real-world data on this topic. Our data further supports the use of DCB-only angioplasty for all sub-groups, with zero adverse device-related outcomes across all specified end-points at 6 months, bringing into question the advice from the recent ESC guidance update.¹¹

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