



Short-term DAPT after coronary stenting has similar ischemic and bleeding outcomes as long-term DAPT: a 5-year population-based cohort study

Sriraag Balaji Srinivasan^{1,2} · Amro Sehly¹ · Biyanka Jaltotage¹ · Simon Qin³ · Abdul Rahman Ihdahid^{1,4,5} · James Marangou^{1,6} · James M. Rankin¹ · Frank M. Sanfilippo³ · Girish Dwivedi^{1,2,4}

Received: 17 September 2022 / Accepted: 20 September 2022 / Published online: 29 September 2022
© The Author(s) 2022

Abstract

Background Optimal duration of dual antiplatelet therapy (DAPT) following percutaneous coronary intervention (PCI) remains controversial.

Aim We investigated the relationship between DAPT duration following PCI and long-term ischemic and bleeding outcomes under real-world conditions.

Methods Patients aged ≥ 65 years who underwent PCI with stenting in Western Australian hospitals between 2003 and 2008 and survived 2 years were identified from linked hospital admissions data. The primary outcome was major adverse cardiovascular and cerebrovascular events (MACCE) defined as a composite of all-cause death and admissions for acute coronary syndrome (ACS), coronary artery revascularization procedure, stroke, and major bleeding. Secondary outcomes were ACS admissions, all-cause death, and major bleeding admissions. Patients were followed up for 5 years from initial PCI.

Results A total of 3963 patients were included in the final analysis. The mean age of the cohort was 74.5 ± 6.1 years with 67.3% males. No significant difference was seen with 6–12, 12–18, or 18–24 months DAPT, compared to 0–6 months DAPT duration for MACCE and all secondary outcomes at 3- and 5-year post-PCI.

Conclusion There is no significant difference in both bleeding and ischemic outcomes in long-term DAPT as compared to short-term DAPT for first- and second-generation drug-eluting stents in a real-world population.

Keywords Bleeding · DAPT · Stenting · Thrombosis

Introduction

Optimal duration of dual antiplatelet therapy (DAPT) following percutaneous coronary intervention (PCI) with stent insertion remains controversial. Randomized trials

have demonstrated that long-term DAPT beyond 1 year results in fewer ischemic events at the expense of greater bleeding events [1, 2]. As such, individualized ischemic and bleeding risks are considered when selecting optimal DAPT duration [3]. However, trial populations are not representative of real-world patients, and their findings should therefore be met with caution. A further layer of complexity is added when developments in stent technology and changes in practice patterns over time are considered; these factors are challenging to capture in rigid protocol-driven clinical trials. Additionally, most trials have shorter follow-up durations, offering limited long-term outcome data. Population-based studies provide large, long-term, real-world data that can address these issues. We investigated the relationship between DAPT duration following PCI and ischemic and bleeding outcomes under real-world conditions.

✉ Girish Dwivedi
girish.dwivedi@perkins.uwa.edu.au

¹ Department of Cardiology, Fiona Stanley Hospital, Perth, WA, Australia

² School of Medicine, University of Western Australia, Perth, WA, Australia

³ School of Population and Global Health, University of Western Australia, Perth, WA, Australia

⁴ Harry Perkins Institute of Medical Research, Perth, WA, Australia

⁵ Medical School, Curtin University, Perth, WA, Australia

⁶ Menzies School of Health Research, Darwin, NT, Australia

Methods

Patients aged ≥ 65 years who had a PCI with stent implantation for any indication in Western Australian (WA) hospitals between 2003 and 2008 and survived 2 years following PCI were identified from linked hospital admissions data. Pharmaceutical Benefits Scheme (PBS) data was used to identify DAPT duration. The PBS is a national Australian Government program that subsidizes the cost of prescription medicine. Demographic and outcome data was obtained from Western Australian Hospital Morbidity Data Collection, Emergency Department Data Collection and Mortality Register databases. Patients were followed up for 3 years (a total of 5 years from initial PCI). The primary outcome of the study was major adverse cardiovascular and cerebrovascular events (MACCE) defined as a composite of all-cause death and admissions for acute coronary syndrome (ACS), coronary artery revascularisation procedure, stroke and major bleeding. Secondary outcomes were ACS admissions, all-cause death, and major bleeding admissions. Patients were stratified into four DAPT duration groups at 6-month intervals, 0–6 months, 6–12 months, 12–18 months and 18–24 months. Adjusted Cox regression analysis was done on outcome data at 3-years post-PCI and 5-years post-PCI, comparing DAPT duration outcomes to the baseline of 0–6 months. Outcome analysis was adjusted based on patient, lesion, and procedure related factors.

Results

A total of 7407 patients underwent coronary stent implantation in WA hospitals between 2003 and 2008, of which 6466 survived 2 years following PCI. A further 2503 were excluded due to unavailable medication records, with a final total of 3963 included in the analysis. The mean age of the cohort was 74.5 ± 6.1 years with 67.3% males. More than half of patients underwent PCI for acute coronary syndrome (53.4%), 19.8% unstable angina, 17.8% non-ST elevation myocardial infarction, and 15.8% ST elevation myocardial infarction. The remaining patients had stable angina (46.6%). A total of 56.4% of patients had single-stent intervention, with the remainder (43.6%) having multiple stents inserted. Drug-eluting stents (DES) comprised 84.1% of all stents used; the other 15.6% was bare metal stents (BMS). All patients were dispensed aspirin and clopidogrel as DAPT. A total of 1158 (29.2%) received DAPT for 0–6 months, 1352 (34.1%) received DAPT for 6–12 months, 1034 (26.1%) received DAPT for 12–18 months, and 419 (10.6%) received DAPT for 18–24 months.

No significant difference was seen with 6–12 months, 12–18 months, or 18–24 months DAPT, compared to 0–6 months DAPT duration for MACCE at 3-year and

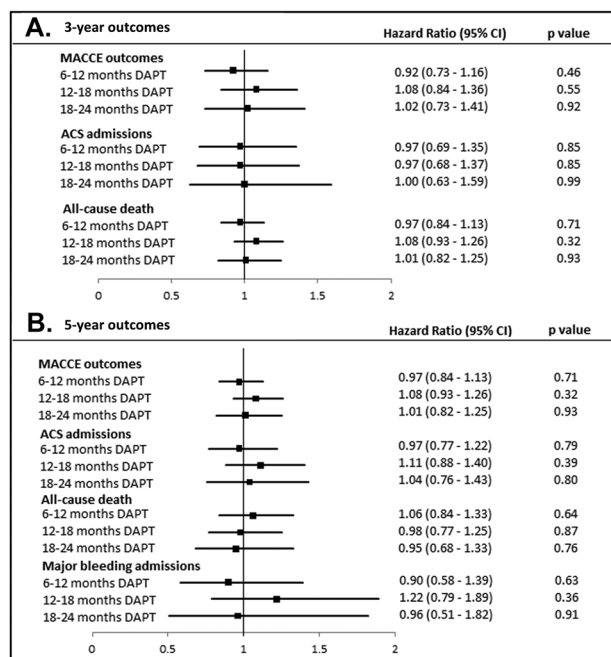


Fig. 1 Results from adjusted Cox regression analyses at 3-years (A) and 5-years (B) post-coronary stent implantation. Hazard ratios (HRs) are with reference to outcomes for 0- to 6-month DAPT. Central boxes represent HRs, and error bars represent 95% confidence intervals. DAPT dual antiplatelet therapy, ACS acute coronary syndrome, MACCE major adverse cardiovascular and cerebrovascular events

5-year post-PCI. No significant difference was seen in ACS admission, all-cause death, and major bleeding outcomes at 3-year and 5-year post-PCI for these groups as compared to 0- to 6-month DAPT duration (Fig. 1).

Discussion

For over a decade, multiple randomised trials have studied the optimal duration of DAPT, yet the answer remains elusive. The landmark DAPT trial established the outcome benefits of long-term DAPT beyond 12 months, with a notable increase in major bleeding admissions [1]. Conversely, the ITALIC trial found no difference between short-term and long-term DAPT, demonstrating no change in thrombotic and bleeding risks in 6 months vs 24 months of DAPT [4]. Meta-analyses have also demonstrated differing results, with more recent data trending towards shorter duration DAPT [5]. These trials lack real-world data and long-term follow-up, a distinct strength of population-based studies.

Our study demonstrated that there was no significant difference in both bleeding and thrombotic outcomes in long-term DAPT as compared to short-term DAPT with predominantly first- and second-generation DES in a real-world population. With the established improvement in

newer generation DES in thrombotic risk, our findings align with other work suggesting low thrombotic risk with short-term DAPT [6]. Conversely, similar bleeding risks provide reassurance in patients requiring prolonged DAPT. This is encouraging in the era of personalized medicine, permitting flexibility in DAPT duration depending on individual thrombotic and bleeding risk. The limitations of our study include its retrospective nature, the age of the data, the use of clopidogrel in contrast to ticagrelor, the high percentage of BMS use, and inherent limitations of database data.

Acknowledgements We thank the following institutions for providing the data used in this study. Staff at the WA Data Linkage Branch and data custodians of the WA Department of Health for access to and provision of the State linked data (Hospital Morbidity Data Collection, Emergency Department Data Collection and Death Registrations). The Australian Department of Health for the cross-jurisdictional linked PBS data. The people of Western Australia whose data were used in this study. This research is supported by a project grant from the National Health and Medical Research Council of Australia (NHMRC project grant 1066242).

Author contribution GD and FS conceived the study. SBS, JM, and FS conducted the study and collected and analyzed the data. SBS, AS, and BJ wrote the first draft of the manuscript. All co-authors critically revised the manuscript and gave final approval and agree to be accountable for all aspects of the work ensuring integrity and accuracy.

Funding Open Access funding enabled and organized by CAUL and its Member Institutions.

Declarations

Ethics approval and consent to participate Ethics approval was obtained from the University of Western Australia Human Research Ethics Committee (UWA HREC RA/4/1/8065) and Western Australia Department of Health Human Research Ethics Committee (RGS2803), and the study was conducted according to the principles of the Declaration of Helsinki.

Conflict of interest BJ consults for the Artrya Pty Ltd. ARI consults and has equity interest in the Artrya Pty Ltd. GD received speaker

bureau fees for Pfizer, Johnson and Johnson, and Amgen and conference sponsorship from Bayer and consults and has equity interest in the Artrya Pty Ltd. The other authors declare no competing interests.

Open Access This article is licensed under a Creative Commons Attribution 4.0 International License, which permits use, sharing, adaptation, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons licence, and indicate if changes were made. The images or other third party material in this article are included in the article's Creative Commons licence, unless indicated otherwise in a credit line to the material. If material is not included in the article's Creative Commons licence and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this licence, visit <http://creativecommons.org/licenses/by/4.0/>.

References

1. Mauri L, Kereiakes DJ, Yeh RW et al (2014) Twelve or 30 months of dual antiplatelet therapy after drug-eluting stents. *N Engl J Med* 371:2155–2166. <https://doi.org/10.1056/NEJMoa1409312>
2. Bonaca MP, Bhatt DL, Cohen M et al (2015) Long-term use of ticagrelor in patients with prior myocardial infarction. *N Engl J Med* 372:1791–1800. <https://doi.org/10.1056/NEJMoa1500857>
3. Lugo LM, Ferreiro JL (2018) Dual antiplatelet therapy after coronary stent implantation: individualizing the optimal duration. *J Cardiol* 72:94–104. <https://doi.org/10.1016/j.jjcc.2018.03.001>
4. Gilard M, Barragan P, Noryani AAL et al (2015) 6- versus 24-month dual antiplatelet therapy after implantation of drug-eluting stents in patients nonresistant to aspirin: the randomized, multicenter ITALIC trial. *J Am Coll Cardiol* 65:777–786. <https://doi.org/10.1016/j.jacc.2014.11.008>
5. Bularga A, Meah MN, Doudesis D et al (2021) Duration of dual antiplatelet therapy and stability of coronary heart disease: a 60 000-patient meta-analysis of randomised controlled trials. *Open Heart* 8:e001707. <https://doi.org/10.1136/openhrt-2021-001707>
6. Bangalore S, Toklu B, Patel N et al (2018) Newer-generation ultrathin strut drug-eluting stents versus older second-generation thicker strut drug-eluting stents for coronary artery disease. *Circulation* 138:2216–2226. <https://doi.org/10.1161/CIRCULATIONAHA.118.034456>

Publisher's Note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.