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Short duration of dual antiplatelet therapy following complex percutaneous coronary intervention: A systematic review and meta-analysis

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ABSTRACT

Introduction and aim: The optimal composition and duration of antiplatelet therapy after complex percutaneous coronary intervention (PCI) remains unclear. We conducted a meta-analysis to compare 1–3 months of dual antiplatelet therapy (DAPT) followed by monotherapy vs. 12 months of DAPT.

Method: MEDLINE/PubMed, EMBASE, and Cochrane Central Register of Controlled Trials were queried for studies comparing 1–3 months of DAPT followed by monotherapy vs. 12 months of DAPT in the outcomes of complex PCI from inception through January 2023. Outcomes of interest included major bleeding, all-cause mortality, cardiovascular mortality, myocardial infarction (MI), stent thrombosis, target vessel revascularization, and stroke.

Results: Compared to 12 months, 1–3 months of dual antiplatelet therapy had a weak association with less major bleeding (OR 0.67; 95 % CI, 0.44–1.00; $p = 0.05$; $I^2 = 28$ %). There were no significant differences between the shorter and longer antiplatelet therapy in terms of all-cause mortality (OR 0.83; 95 % CI, 0.59–1.16; $p = 0.21$; $I^2 = 17$ %), cardiovascular mortality (OR 0.87; 95 % CI, 0.53–0.42; $p = 0.50$; $I^2 = 0$), MI (OR 0.97; 95 % CI, 0.69–1.35; $p = 0.82$; $I^2 = 32$ %), stent thrombosis (OR 1.17, 95 % CI, 0.77–1.76; $p = 0.38$; $I^2 = 0$ %), target vessel revascularization (OR 1.05, 95 % CI, 0.58–1.89; p = 0.82; $I^2 = 64$ %), or stroke (OR 1.10, 95 % CI, 0.55–2.17; $p = 0.37$; $I^2 = 7$ %);.

Conclusion: Among patients undergoing complex PCI, DAPT for 1–3 months may be associated with less major bleeding but similar rates of cardiovascular events (death, MI, stroke, stent thrombosis, and revascularization) compared to DAPT for 12 months.

1. Introduction

Dual antiplatelet therapy (DAPT) is the cornerstone of medical management after percutaneous coronary intervention (PCI) to decrease the risk of stent thrombosis as well as unrelated ischemic cardiovascular events. The optimal duration of DAPT is a matter of on-going debate. Current guidelines recommend at least 12 months of DAPT after PCI for acute coronary syndrome (ACS) and six months after non-ACS-PCI [1,2]. The relative thrombotic and bleeding risks after PCI must guide the specific composition and duration of antiplatelet therapy.

Complex PCI is associated with a considerable risk of subsequent thrombotic complications. Studies frequently define complex PCI as procedures with at least one of the following criteria: 3 vessels treated, ≥3 stents implanted, ≥3 lesions treated, bifurcation lesion with 2 stents

Abbreviations: PCI, Percutaneous Coronary Intervention; ST, Stent thrombosis; ACS, Acute Coronary Syndrome; DAPT, Dual antiplatelet therapy.

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implanted, total stent length > 60 mm, or chronic total occlusion. Other studies have also included in the definition of complex PCI those interventions involving the left main or proximal left anterior descending (LAD) coronary arteries, bypass grafts, thrombus-containing lesions, and lesion length > 30 mm [4]. Potent antiplatelet therapy for an extended duration has been hypothesized to reduce the risk of adverse events in these high-risk lesions and interventions. However, extended, potent antiplatelet therapy may also convey a higher risk of bleeding.

Randomized controlled trials (RCTs) have assessed the safety and efficacy of short-duration (1–3 months) DAPT in patients with ACS and chronic ischemic heart disease [5–7]. The MASTER DAPT trial compared the shortest durations of DAPT use (1 vs. 3 months) in patients with high bleeding risk (HBR) and showed fewer bleeding events and non-inferiority in preventing thrombotic events with 1 month of DAPT [8]. However, data on short DAPT in patients undergoing complex PCI are limited. Hence, we conducted this meta-analysis to study the outcomes of 1–3 months of DAPT vs. 12 months of DAPT in patients undergoing complex PCI.

2. Methods

The present meta-analysis was performed in accordance with Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines and the Cochrane Collaboration Handbook [9]. The study was registered in the PROSPERO (International Prospective Register of Systematic Reviews) Registry.

2.1. Search strategy and study selection

Two independent reviewers (MM, MRM) conducted a literature search of electronic databases including MEDLINE/PubMed, EMBASE, and the Cochrane Central Register of Controlled Trials without language limitations from database inception through January 2023. We also searched Google Scholar and two clinical trial registries (the World Health Organization's International Clinical Trials Registry Platform and ClinicalTrials.gov). The references of the retrieved studies were screened for additional studies appropriate for this meta-analysis. The search included the following query terms: ("Dual antiplatelet" OR "DAPT") AND ("Complex intervention" OR "percutaneous coronary intervention") AND ("aspirin" OR "ticagrelor" OR "monotherapy" OR "clopidogrel"). There were no restrictions on sample size or follow-up duration. Studies were considered eligible for inclusion in the meta-analysis if they met pre-determined inclusion criteria: (1) Studies evaluating 1–3 month versus 12-month courses of DAPT; (2) Studies enrolling patients undergoing complex PCI; and (3) Studies evaluating cardiovascular outcomes. RCTs and observational studies were included. Editorials, reviews, and non-human studies were excluded.

2.2. Screening, data extraction and quality assessment

Initial title and abstract screening were conducted by two reviewers (MM, MRM), and discrepancies were resolved by a third reviewer (MN). Potentially eligible studies underwent full-text review and assessment for inclusion. Study and patient characteristics and outcomes data were extracted into a spreadsheet. Study and patient characteristics data included first author's name, study design, study country, sample size, complex PCI definition, median age, percentage of male subjects, hypertension, diabetes, dyslipidemia, acute coronary syndrome, type of stent, DAPT duration, and DAPT composition. Two authors (MN, SM) independently assessed the quality of studies and risk of bias (Supplementary Table 1 and Supplementary Fig. 1-A & 1-B).

2.3. Outcomes

Outcomes of interest included major bleeding, all-cause mortality, cardiovascular mortality, myocardial infarction (MI), stent thrombosis, target vessel revascularization, and stroke. Outcomes were defined by the individual studies.

2.4. Statistical analysis

We pooled outcomes using inverse variance random-effects models. We used the Paule–Mandel method for estimation of τ^2. Hartung–Knapp/Sidik-Jonkman small-sample adjustments were applied because the number of studies was <10 [3]. We reported effect sizes as odds ratios (ORs) with 95 % confidence intervals (CIs). Statistical significance was defined as $p < 0.05$. We used I^2 statistics to measure heterogeneity ($I^2 > 50$ % was considered a high degree of heterogeneity). Publication bias was not assessed due to the small number of the included studies. Sensitivity analyses were performed by excluding one trial at a time and repeating the analyses. All analyses were performed using R version 4.0.3 meta package.

3. Results

3.1. Summary of the studies

The initial search identified a total of 1119 studies. After title and abstract screening, 29 studies underwent full text review based upon our inclusion criteria. Seven studies, all RCTs, met inclusion criteria and were included in the meta-analysis [10–16]. A total of 12,278 patients were included in our final pooled analysis of whom 6095 were treated with 1–3 months of DAPT and 6183 patients were treated with 12 months of DAPT. The search process is outlined in Fig. 1.

The baseline characteristics of the patients in each study are reported in Table 1. Mean ages were 63–73 years, and 70–80 % of patients were male. The length of follow-up ranged from 12 to 24 months. The antiplatelet regimens in each study are presented in (Table 2). Criteria defining complex PCI for each study are presented in Table 3. In general, complex PCI was defined by at least one of the following angiographic characteristics: 3 vessels treated, ≥3 stents implanted, ≥3 lesions treated, bifurcation PCI with ≥2 stents, and a total stent length of ≥60 mm, use of any atherectomy device, left main as target vessel, surgical bypass graft or chronic total occlusion as target lesions.

3.2. Outcomes

There was borderline reduction in major bleeding (OR 0.67; 95 % CI, 0.44–1.00; $p = 0.05$; $I^2 = 28$ %) among the 1–3 month DAPT group compared with the 12 month DAPT group (Fig. 2). There were no significant difference between the groups in terms of all-cause mortality (OR 0.83; 95 % CI, 0.59–1.16; $p = 0.21$; $I^2 = 17$ %); cardiovascular mortality (OR 0.87; 95 % CI, 0.53-a.42; $p = 0.50$; $I^2 = 0$); myocardial infarction (OR 0.97; 95 % CI, 0.69–1.35; $p = 0.82$; $I^2 = 32$ %); stroke (OR 1.10, 95 % CI, 0.55–2.17; $p = 0.37$; $I^2 = 7$ %); stent thrombosis (OR 1.17, 95 % CI, 0.77–1.76; $p = 0.38$; $I^2 = 0$ %) or target vessel revascularization (OR 1.05, 95 % CI, 0.58–1.89; p = 0.82; $I^2 = 64$ %) **(Figs. 2-B to 2-G)**. In leave-one-out sensitivity analyses, the omission of Serruys et al. [13]. made short DAPT significantly associated with a lower risk of major bleeding (OR 0.55, 95 % CI, 0.37–0.83; $I^2 = 0$ %). Omitting other studies at a time and repeating the analysis showed no significant difference between the DAPT regimens in terms of major bleeding. Leave-one-out sensitivity analyses did not show significant changes in all-cause mortality, cardiovascular mortality, myocardial infarction, stroke, stent thrombosis or target vessel revascularization (Supplementary Figs. 2-A to 2-G).

4. Discussion

In our meta-analysis of 7 RCTs including 12,278 patients undergoing complex PCI, we found that DAPT for 1–3 months was weakly associated with less major bleeding compared with DAPT for 12 months.

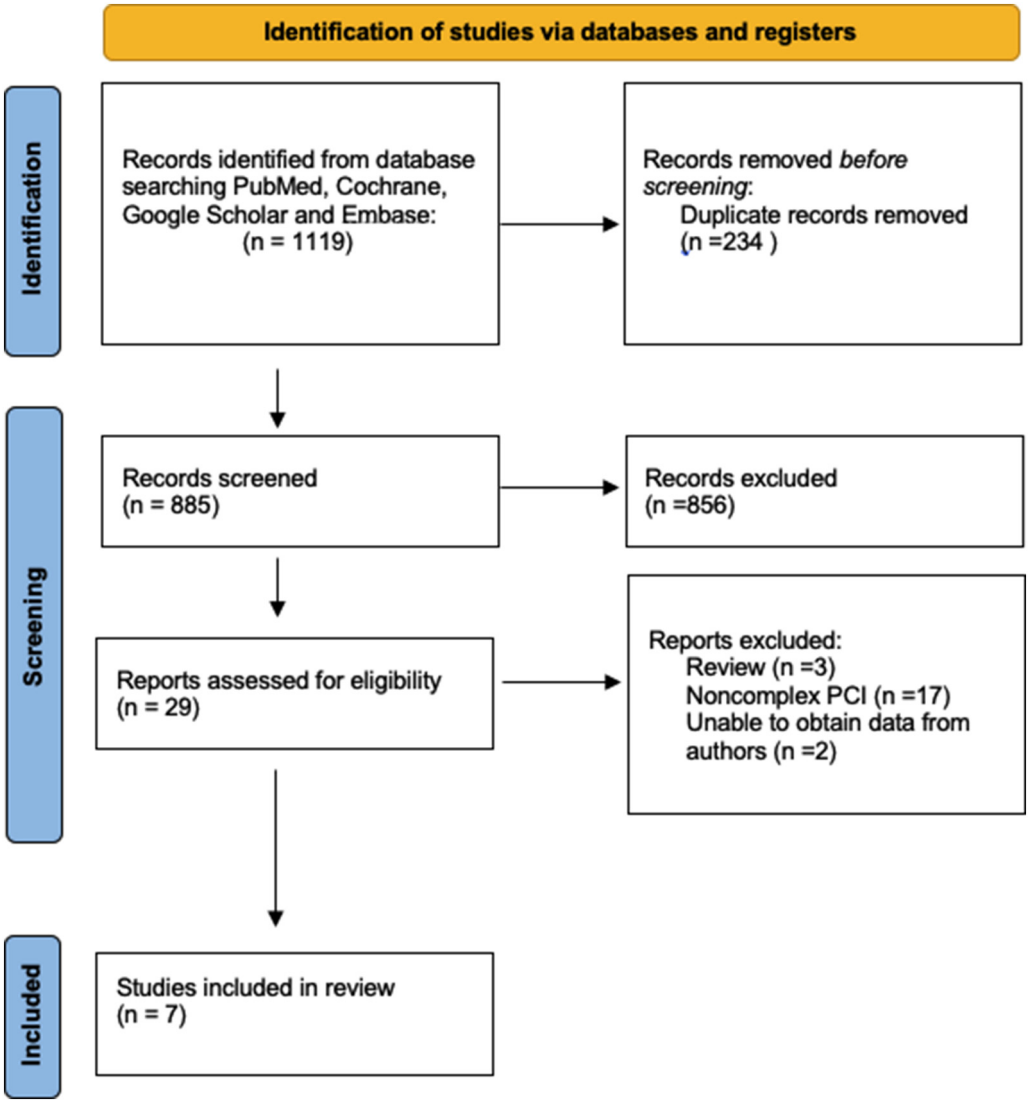

Fig. 1. PRISMA flow diagram.

There were no differences in all-cause mortality, cardiovascular mortality, myocardial infarction, stent thrombosis, stroke, or target vessel revascularization.

4.1. Mortality, stroke, myocardial infarction and revascularization

Our analysis did not find a statistical difference between short DAPT (1–3 months) and extended DAPT (12 months) in terms of mortality, MI, stroke and target vessel revascularization. These findings are consistent with recent studies showing the effectiveness of dual therapy for one month. The STOPDAPT-2 trial randomly assigned 3045 patients undergoing PCI to receive either 12 months of DAPT (aspirin and clopidogrel) or 1 month of DAPT, followed by clopidogrel monotherapy [17]. The 1-month DAPT showed similar protection against CV mortality, MI, ischemic or hemorrhagic stroke, and stent thrombosis. This brief DAPT was also effective in preventing serious bleeding incidents. A number of publications combined data from large trials to examine the effects of short DAPT in complex PCI because no major studies exclusively enrolled these high risk patients. A subgroup analysis of the STOPDAPT-2 study pooled data from 509 patients who underwent complex coronary interventions [15]. The study found that the clopidogrel monotherapy after one month of clopidogrel-based DAPT has

Table 1
Baseline characteristics of patients undergoing complex PCI.

Study	Age	Men %	HTN %	DM %	HLD %	Smoking %	ACS %	Prior MI %
Valgimigli 2022 [10]	76.51 + 8.17	70	78	34	69	7	N.A	22
Dangas 2020 [11]	66.0 ± 10.4	79	71.2	37	58.2	N.A	63	28.7
Roh 2021 [12]	64.4 ± 10.7	75.5	68.3	43.8	44.6	127 (25.5 %)	57.8	3.6
Serruys 2019 [13]	65.3 ± 10.3	78	73	26	68	26	48	21
Lee 2021 [14]	63.0 ± 10.6	76	60	56	63	N.A	100	4
Yamamoto 2021 [15]	69.5 ± 10.1	80	76.2	47.7	79.2	N.A	32.2	17.7
Giustino 2016 [16]	63.6 ± 10.8	68.7	74.6	35.8	65.5	26.5	47.4	20.5

Table 2
Included studies characteristics.

Study	Country	Sample Size	Design	Short DAPT (1–3 months)	Extended DAPT (12 months)	Stent type	Follow up
Valgimigli 2022 [10]	Europe, Japan, Asia, Australia and Latin America	1196	Master DAPT RCT sub-analysis	1 month	≥ 3 months	Bioresorbable Polymer-Coated Ultimaster™ (Terumo Corporation, Tokyo, Japan) sirolimus-eluting stent	12 months
Dangas 2020 [11]	North America, Europe, and Asia	7119	Pooled from TWILIGHT RCT	3 months of DAPT (ASA + Ticagrelor) followed by Ticagrelor alone	12 months	drug-eluting stent	15 months
Roh 2021 [12]	East Asia	2993	A post-hoc analysis of SMART-CHOICE RCT	3 months of DAPT (ASA + P2Y12 inhibitor), followed by 9 months of P2Y12 inhibitor monotherapy	12 months	Ultrathin Sirolimus-Eluting Stents With Biodegradable Polymer (Orsiro)	12 months
Serruys 2019 [13]	Europe, Australia, Brazil, Canada & Singapore	15,450	A post-hoc analysis of Global Leaders RCT	1-month DAPT (ASA + ticagrelor) followed by 23- month ticagrelor monotherapy	12 months DAPT (Plavix or Ticagrelor) followed by 12 months of aspirin monotherapy	Biolimus A9-eluting stents (BES) (BioMatrix, Biosensors, Europe)	24 months
Lee 2021 [14]	South Korea	3056	A post hoc analysis of TICO RCT	3-months DAPT followed by Ticagrelor monotherapy	12 months of DAPT based ticagleror	ultrathin-strut, bioresorbable-polymer, sirolimus-eluting Orsiro stent (Biotronik)	12 months
Yamamoto 2021 [15]	Japan	3009	post hoc subgroup analysis of STOPDAPT-2 trial	1-month DAPT followed by clopidogrel monotherapy	12 months	cobalt-chromium everolimus-eluting stent	12 months
Giustino 2016 [16]	USA	9577	post hoc patient-level pooled analysis of 6 RCTs: PRODIGY, optimize, RESET, EXCELLENT, SECURITY, ITALIC	3 months of DAPT (ASA and Plavix) followed by SAPT	≥ 12 months	new-generation DES	median follow-up time of 392 days (interquartile range: 366 to 710 days)

equivalent efficacy in reducing cardiovascular events with significantly reduced bleeding. Notably, there was no difference in outcomes between complex and non-complex PCI after short DAPT. A post hoc analysis of the Global Leader trial assessed 4570 patients undergoing complex coronary interventions [13]. Patients were randomized to DAPT for one month, followed by ticagrelor monotherapy for 23 months and 12 months of aspirin after 12 months of DAPT. Ticagrelor monotherapy reduced all-cause mortality, new myocardial infarction, and fewer bleeding events. The main benefit of ticagrelor monotherapy after aspirin cessation was observed in patients who underwent PCI for acute coronary syndrome. Moreover, a subgroup analysis of 2342 patients from the TWILIGHT study who were undergoing complex PCI showed that ticagrelor monotherapy followed by three months of aspirin co-administration is associated with a significantly lower risk of bleeding and a similar level of protection from death, MI, stroke, and stent thrombosis compared to ticagrelor-based DAPT [11].

In a similar vein, Rout et al. conducted a comprehensive meta-analysis encompassing 11 randomized controlled trials (RCTs) with approximately 48,000 patients. Their analysis demonstrated that for patients undergoing current-generation DES implantation, adopting short-term DAPT for a duration of 1–3 months reduces the occurrence of major bleeding without leading to an increase in ischemic events, as compared to long-term DAPT [18]. Another noteworthy meta-analysis, conducted by Mankerious et al., incorporated data from 6 studies involving roughly 15,000 patients. Their findings concluded that employing short-term DAPT following PCI in patients at a high bleeding risk was associated with a significant reduction in major bleeding events and similar ischemic outcomes [19]. Furthermore, an analysis undertaken by Tsigkas et al. encompassed 8 RCTs, involving approximately 41,000 patients. This study determined that adopting very short-term DAPT (<3 months) resulted in a notable decrease in the odds of net adverse clinical events and major bleeding, with reductions of 17 % and 29 %, respectively, without an associated increase in ischemic events [20]. It's important to note that while these studies did not exclusively focus on complex PCI procedures and patients at a high risk of ischemia, their findings align closely with the outcomes of our own meta-analysis.

4.2. Major bleeding

The high bleeding risk (HBR) and complexity of the intervention are the primary determinants of the decision to deescalate antiplatelet therapy after PCI. Clinical research demonstrated that patients with HBR benefited from short-term DAPT. A post hoc analysis of the STOPDAPT-2 trial pooled data from 1054 patients with high bleeding risk and followed the same protocol as the STOPDAPT-2. One-month DAPT significantly reduced major bleeding without any increase in cardiovascular events over 12-month of DAPT in HBR patients [21]. A study by Mehran et al. enrolled 3652 patients with HBR to receive DAPT for 1–3 months or 6–12 months. The primary endpoint of mortality and myocardial infarction were similar between the two groups. The bleeding events were generally less in the short DAPT group, but statistical significance was met only for major bleeding [22]. An interesting subgroup analysis of the STOPDAPT-2 trial studied the effect of HBR and complex PCI on the selection of short or standard DAPT. The absolute benefit of a 1-month of DAPT in reducing bleeding events was observed in patients with HBR. Surprisingly, patients without high bleeding risk did not benefit from the short duration of DAPT, and there was no difference in the primary cardiovascular endpoints between complex and non-complex PCI [23]. Although our study found that the 1–3 months of DAPT is associated with fewer bleeding events than the standard therapy, this did not reach statistical significance. The most plausible explanation is that most pooled data were not on high bleeding risk patients. Secondly, the number of bleeding events was low, which may overestimate the effect.

Last but not least, there is debate and limited evidence about the ideal antiplatelet monotherapy following de-escalation from DAPT. The most widely used $P2Y_{12}$ inhibitors in patients with acute coronary

Table 3
Criteria of complex PCI per each included study.

Study	Complex PCI def
Valgimigli 2022 [10]	At least one of the following angiographic characteristics: 1- three vessels treated 2- ≥3 stents implanted 3- ≥3 lesions treated 4- bifurcation with two stents implanted 5- total stent length 0.60 mm 6- chronic total occlusion as target lesion. 7- left main or graft intervention
Dangas 2020 [11]	at least 1 of the following characteristics: 1- ≥3 vessels treated 2- ≥3 lesions treated 3- total stent length > 60 mm 4- bifurcation with 2 stents implanted 5- use of any atherectomy device 6- left main as target vessel OR surgical bypass graft 7- chronic total occlusion as target lesions
Roh 2021 [12]	At least one of the following angiographic characteristics: 1- ≥3 vessels treated, 2- ≥ 3 stents implanted 3- ≥ 3 lesions treated 4- Bifurcation PCI with ≥2 stents. 5- Total stent length of ≥60 mm.
Serruys 2019 [13]	At least one of the following features were met; 1- multivessel PCI, 2- ≥3 stents implanted, 3- ≥3 lesions treated, 4- Bifurcation PCI with >_ 2 stents. 5- Total stent length > 60 mm
Lee 2021 [14]	At least one of the following: 1- Number of stents implanted ≥3, 2- Number of lesions treated ≥3 3- ≥3vessels treated 4- Bifurcation PCI with 2 stents, 6- Total stent length ≥ 60 mm 7- Chronic total occlusion.
Giustino 2016 [15]	At least 1 of the following angiographic characteristics: 1- ≥3 vessels treated, 2- ≥3 stents implanted, 3- ≥3 lesions treated, 4- bifurcation with 2 stents implanted. 5- total stent length > 60 mm. 6- chronic total occlusion as target lesion
Yamamoto 2021 [16]	At least one of the following procedural criteria: 1- 3 vessels treated. 2- ≥3 stents implanted. 3- ≥3 lesions treated. 4- bifurcation with 2 stents implanted. 5- total stent length > 60 mm. 6- chronic total occlusion as the target lesion.

syndrome with or without PCI are clopidogrel, prasugrel, and ticagrelor. Clopidogrel has a number of drawbacks such as the delayed onset of action (2–4 h), a modest degree of platelet inhibition (45–50 %) and interpatient variability [24,25]. Prasugrel and ticagrelor, on the other hand, have a faster onset of action (30 min) and a considerable degree of platelet inhibition (70–75 %). The TRITON–TIMI study compared the efficacy of prasugrel versus clopidogrel in patients with ACS scheduled for PCI. It showed a significant decrease in ischemic events, including stent thrombosis, but the bleeding events were higher with prasugrel [23]. The PLATO trial compared ticagrelor to clopidogrel in patients with ACS, and ticagrelor was associated with a substantial reduction in death, MI, stroke and bleeding. Understanding these variabilities of the antiplatelet potency is essential in the de-escalation, and monotherapy with novel $P2Y_{12}$ inhibitors seems more protective. However, large clinical trials are required to compare their efficacy in patients undergoing complex PCI.

4.3. Future directions

Ultimately, an adequately-powered RCT comparing 1–3-month DAPT vs. 12-month DAPT in complex PCI patients will be necessary to determine the optimal duration of DAPT for these patients. For the sake of feasibility, this study may be a pre-specified subgroup analysis of a larger RCT. Also, the study would preferably be conducted in HBR complex PCI patients to facilitate determination of differences in bleeding risks between the DAPT regimens.

4.4. Limitations

Several study limitations were unavoidable in this meta-analysis. First, there was variability in the antiplatelet regimen among the included trials. Three studies employed ticagrelor-based DAPT, then ticagrelor monotherapy. Three other studies used clopidogrel-based DAPT followed by clopidogrel monotherapy. DAPT was prescribed in one study at the providers' discretion (Table 2). Prasugrel-based short DAPT has not been rigorously studied.

Second, there was variability in the studies' definitions of complex PCI. Two of the included studies identified left main target lesion and bypass graft intervention as complex procedures (Table 3).

Third, patients in the included studies had average bleeding risk.

5. Conclusions

Among patients undergoing complex PCI, DAPT for 1–3 months may be associated with less major bleeding but similar rates of cardiovascular events (death, MI, stroke, stent thrombosis, and revascularization) compared to DAPT for 12 months.

Data availability

Data underlying this article are available in the article and in its online supplementary material.

Declaration of competing interest

Dr. Andrew M. Goldsweig is a consultant at Inari Medical and receives speaking fees from Philips, Edwards.

Dr. Mostafa Reda Mostafa has no conflict of interest to disclose.
Dr. Mohamed Magdi Eid has no conflict of interest to disclose.
Dr. Ahmad Al-abdouh has no conflict of interest to disclose.
Dr. Mostafa Najim has no conflict of interest to disclose.
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Dr. Karim M.Al-Azizi has no conflict of interest to disclose.
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Dr. Abdul Rahman Ziada has no conflict of interest to disclose.
Dr. Andrew M. Goldsweig is a consultant at Inari Medical and receives speaking fees from Philips, Edwards.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.carrev.2023.11.002.

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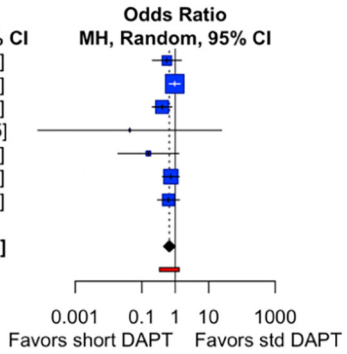
A: The forest plot of major bleeding

Study	Short DAPT Events	Short DAPT Total	Std DAPT Events	Std DAPT Total	Weight	Odds Ratio MH, Random, 95% CI
Giustino et al. 2016	6	826	11	854	9.2%	0.56 [0.21; 1.52]
Serruys et al. 2019	55	2283	57	2287	35.3%	0.97 [0.66; 1.41]
Dagnas et al. 2020	12	1158	30	1184	17.3%	0.40 [0.21; 0.79]
Roh et al. 2021	0	260	2	238	0.3%	0.04 [0.00; 24.65]
Yamamoto et al. 2021	1	245	7	274	2.3%	0.16 [0.02; 1.28]
Lee et al. 2021	20	735	27	738	21.1%	0.74 [0.41; 1.33]
Valgimigli et al. 2022	11	588	18	608	14.5%	0.62 [0.29; 1.33]
Total (95% CI)		**6095**		**6183**	**100.0%**	**0.67 [0.44; 1.00]**
Prediction interval						**[0.34; 1.31]**

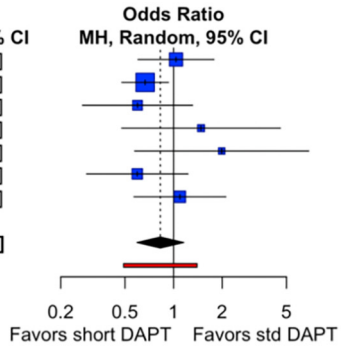
Heterogeneity: $Tau^2 = 0.0420$; $Chi^2 = 8.37$, df = 6 (P = 0.21); $I^2 = 28\%$
Test for overall effect: $t_6 = -2.44$ (P = 0.05)



B: The forest plot of all-cause mortality

Study	Short DAPT Events	Short DAPT Total	Std DAPT Events	Std DAPT Total	Weight	Odds Ratio MH, Random, 95% CI
Giustino et al. 2016	27	826	27	854	18.7%	1.04 [0.60; 1.78]
Serruys et al. 2019	60	2283	89	2287	36.0%	0.67 [0.48; 0.93]
Dagnas et al. 2020	10	1158	17	1184	10.1%	0.60 [0.27; 1.31]
Roh et al. 2021	8	260	5	238	5.2%	1.48 [0.48; 4.59]
Yamamoto et al. 2021	7	245	4	274	4.4%	1.99 [0.57; 6.87]
Lee et al. 2021	12	735	20	738	11.7%	0.60 [0.29; 1.23]
Valgimigli et al. 2022	19	588	18	608	13.8%	1.09 [0.57; 2.11]
Total (95% CI)		**6095**		**6183**	**100.0%**	**0.83 [0.59; 1.16]**
Prediction interval						**[0.49; 1.40]**

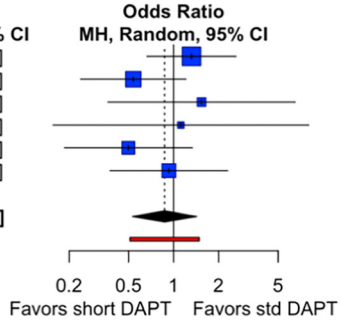
Heterogeneity: $Tau^2 = 0.0229$; $Chi^2 = 7.26$, df = 6 (P = 0.30); $I^2 = 17\%$
Test for overall effect: $t_6 = -1.39$ (P = 0.21)



C: The forest plot of cardiovascular mortality

Study	Short DAPT Events	Short DAPT Total	Std DAPT Events	Std DAPT Total	Weight	Odds Ratio MH, Random, 95% CI
Giustino et al. 2016	19	826	15	854	32.2%	1.32 [0.66; 2.61]
Dagnas et al. 2020	9	1158	17	1184	22.8%	0.54 [0.24; 1.21]
Roh et al. 2021	5	260	3	238	7.2%	1.54 [0.36; 6.50]
Yamamoto et al. 2021	2	245	2	274	3.9%	1.12 [0.16; 8.01]
Lee et al. 2021	6	735	12	738	15.5%	0.50 [0.19; 1.33]
Valgimigli et al. 2022	9	588	10	608	18.3%	0.93 [0.37; 2.30]
Total (95% CI)		**3812**		**3896**	**100.0%**	**0.87 [0.53; 1.42]**
Prediction interval						**[0.51; 1.48]**

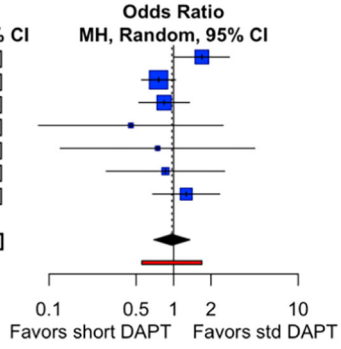
Heterogeneity: $Tau^2 = 0$; $Chi^2 = 4.67$, df = 5 (P = 0.46); $I^2 = 0\%$
Test for overall effect: $t_5 = -0.73$ (P = 0.50)



D: The forest plot of myocardial infarction

Study	Short DAPT Events	Short DAPT Total	Std DAPT Events	Std DAPT Total	Weight	Odds Ratio MH, Random, 95% CI
Giustino et al. 2016	40	826	25	854	19.4%	1.69 [1.01; 2.81]
Serruys et al. 2019	71	2283	93	2287	34.4%	0.76 [0.55; 1.04]
Dagnas et al. 2020	33	1158	40	1184	21.8%	0.84 [0.53; 1.34]
Roh et al. 2021	2	260	4	238	2.4%	0.45 [0.08; 2.50]
Yamamoto et al. 2021	2	245	3	274	2.1%	0.74 [0.12; 4.49]
Lee et al. 2021	6	735	7	738	5.4%	0.86 [0.29; 2.57]
Valgimigli et al. 2022	23	588	19	608	14.5%	1.26 [0.68; 2.34]
Total (95% CI)		**6095**		**6183**	**100.0%**	**0.97 [0.69; 1.35]**
Prediction interval						**[0.56; 1.69]**

Heterogeneity: $Tau^2 = 0.0280$; $Chi^2 = 8.78$, df = 6 (P = 0.19); $I^2 = 32\%$
Test for overall effect: $t_6 = -0.23$ (P = 0.82)



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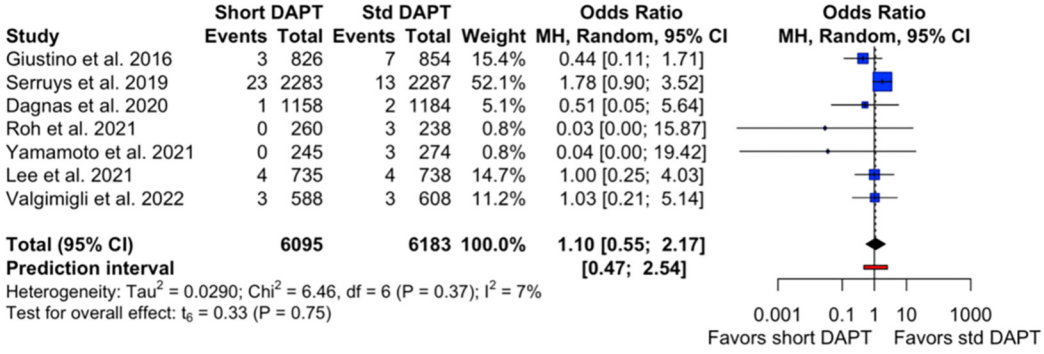
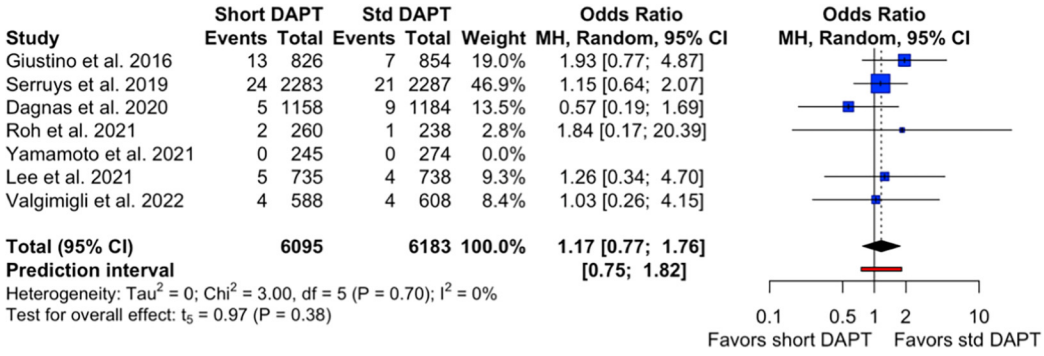
E: The forest plot of stroke



F: The forest plot of stent thrombosis



G: The forest plot of target vessel revascularization

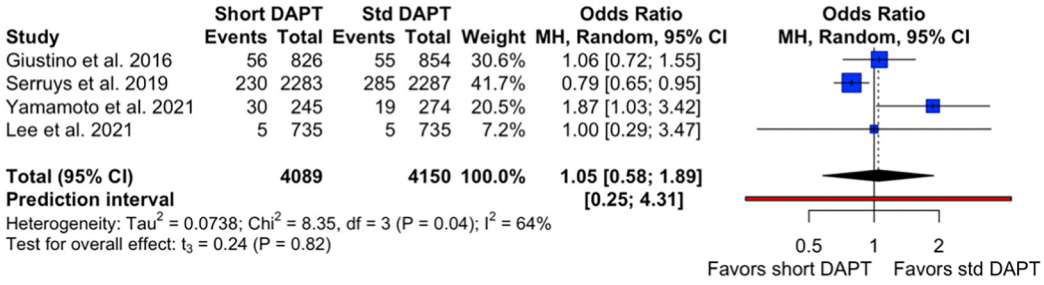


Fig. 2. A: The forest plot of major bleeding
B: The forest plot of all-cause mortality
C: The forest plot of cardiovascular mortality
D: The forest plot of myocardial infarction
E: The forest plot of stroke
F: The forest plot of stent thrombosis
G: The forest plot of target vessel revascularization.

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