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1 Month Dual Antiplatelet Therapy Post Percutaneus Coronary Intervention: A Systematic Review

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Abstract

Background: *Given the advancement of new technologies in the development of coronary stents, the dilemma of the optimal duration of dual antiplatelet therapy (DAPT; Dual Antiplatelet Therapy) subsequent to percutaneous coronary intervention arises, whose safety balance between ischemic and hemorrhagic risks with high mortality.*

Objective: *To analyze experimental evidence on clinical efficacy and safety of DAPT 1 month compared to standard DAPT (≥6 months).*

Method: *Systematic search in Pubmed, Web of Science, Embase and Scopus platforms carried out by four reviewers. The terms "Platelet Aggregation Inhibitors", "Drug-Eluting Stents" and "Percutaneous Coronary Intervention" were used, appended by the operator "AND", the first concept being replaced by "Antithrombocytic agent" exceptionally in the Embase platform. Randomized clinical trials were included in a population older than 18 years, from 2018 to 2022. Articles with enrolled patients not treated with DES, duration of DAPT different from the objective of the review, and studies with endpoints not focused on comparing clinical outcomes between both durations of DAPT were excluded.*

Results: *From the systematic search, 533 results were obtained, of which four articles were included for the purposes of this review. These were aimed at evaluating in some cases the non-inferiority and in others the superiority of 1-month DAPT compared to standard DAPT, concerning adverse clinical events occurring in a certain time according to each clinical trial. Of the four studies reviewed, three studies reported non-inferiority results for 1-month DAPT over standard DAPT for various clinical outcomes. Two of four studies obtained superiority results of 1-month DAPT with fewer adverse clinical events.*

Conclusion: *There is evidence of the non-inferiority of 1-month DAPT compared to standard DAPT after percutaneous coronary intervention in patients with coronary disease, in relation to safety and efficacy, however, more studies are necessary to determine its superiority.*

Keywords: *Platelet aggregation inhibitors; Percutaneous coronary intervention; Drug-eluting stents; Coronary artery disease; Death; Ischemia; Hemorrhage.*

Abbreviations

DAPT: Dual Antiplatelet Therapy.

PCI: Percutaneous Coronary Intervention.

ACS: Acute Coronary Syndrome.

CCS: Chronic Coronary Syndrome.

DES: Drug Eluting Stent.

BMS: Bare Metal Stent.

BARC: Bleeding Academic Research Consortium.

CoCr-EES: Cobalt-Chromium Everolimus-Eluting Stent.

CV: cardiovascular, AMI: Acute Myocardial Infarction.

CVA: Cerebrovascular Attack.

PF-DCS: Polymer free drug-coated stent.

BP-DES: Biopolymer drug eluting stent.

Introduction

Percutaneous coronary intervention (PCI; Percutaneous Coronary Intervention) is one of the most used therapy alternatives in patients with coronary disease, both in acute coronary syndrome (ACS) and in chronic coronary syndrome (CCS). Antiplatelet treatment after the intervention is relevant in the prevention of local and systemic complications. (1)

Dual Antiplatelet Therapy (DAPT) of aspirin in combination with a P2Y12 inhibitor is the evidence-recommended cornerstone of antithrombotic therapy in patients undergoing PCI, whose primary consideration is the balance of risk between bleeding and ischemic events. In the last 4 decades, this antiplatelet treatment has evolved, in which until a few years ago the only P2Y12 inhibitors were clopidogrel and ticlopidine, with more potent inhibitors such as prasugrel, ticagrelor, and more recently cangrelor being introduced around a decade ago. These agents are part of the basket of antithrombotic drugs that also includes aspirin and glycoprotein IIb/IIIa inhibitors, among others, creating a spectrum of combinations available to patients going for PCI. (2)

Despite the development of new, more potent and effective therapies, unanswered questions remain regarding the optimal antiplatelet therapy after PCI. The optimal duration of DAPT is still uncertain, however, its considerations should include the individual risk of the patient regarding the clinical profile, ischemic and hemorrhagic potential, characteristics of the stent used as well as technical and procedural characteristics of the coronary intervention. (3)

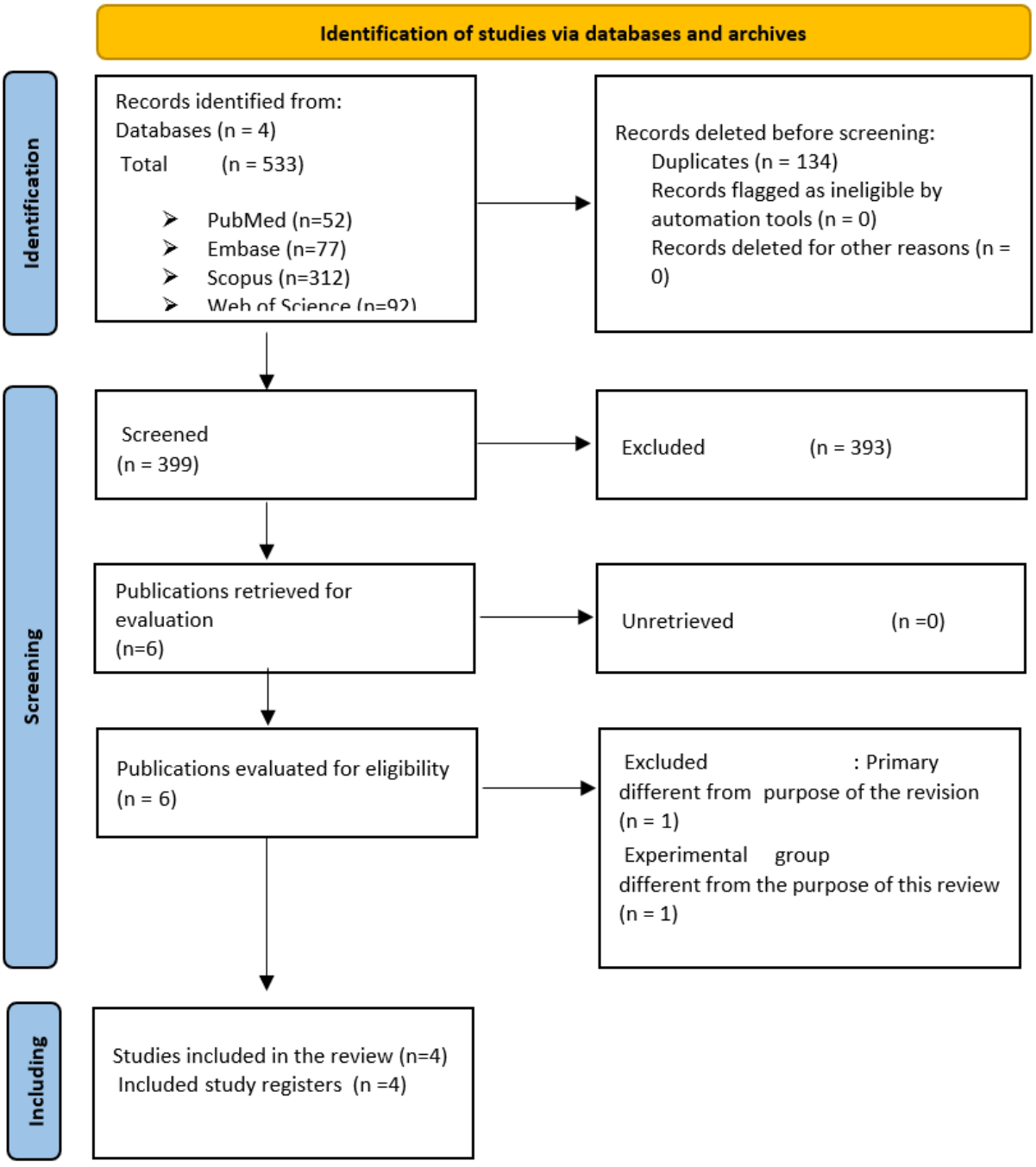
The European Society of Cardiology suggests that in patients with stable coronary disease who have undergone PCI, the duration of DAPT should be 1-6 months, depending on the bleeding risk and regardless of the type of stent used. However, for patients whose ischemic risk prevails over hemorrhagic risk, a longer duration of DAPT may be considered. On the other hand, DAPT for patients with ACS should last 12 months. It can also be administered for a duration of 6 months for patients at high bleeding risk or a duration exceeding 12 months for patients with ACS who have tolerated DAPT without experiencing bleeding complications. (4) For their part, the guidelines issued by the American College of Cardiology and the American Heart Association recommend that a minimum duration of 12 months of should be cases; however, in patients with stable coronary disease, treated with DES, the recommended duration of DAPT has been decreased to 6 months. (5)

Method

This systematic review has been carried out following the recommendations of the PRISMA statement (Preferred Reporting Items for Systematic Reviews and Meta-Analyses). A search for scientific articles was carried out in the MEDLINE (PubMed), Web of Science, Embase and Scopus databases. The search was carried out independently by three reviewers (I.E, B.V and B.M) during the month of July 2022. The MeSH terms "Platelet Aggregation Inhibitors", "Drug-Eluting Stents" and "Percutaneous Coronary Intervention" were used which were appended by means of the boolean operator "AND". Exceptionally, in the Embase platform, due to its own terminology, the term "Platelet Aggregation Inhibitors" was replaced by "Antithrombocytic Agent". The results obtained were delimited to publications of the Clinical Trial type, carried out on a population older than 18 years and no older than 5 years. The selection process was carried out by four reviewers (C.O, I.E, B.V, B.M). Duplicate articles were identified and discarded among the searches carried out in the databases, followed by elimination of articles based on reading the abstract and full text. Randomized clinical trials in patients treated with with drug-eluting stents presenting with ACS or CCS were included, randomized to standard or 1-month DAPT regimens, with no restriction on post-DAPT monotherapy. Articles not published in English, enrolled patients treated with bare metal stents (BMS), DAPT durations other

than those mentioned, studies not focused on comparing clinical endpoints between different DAPT durations were excluded.

The variables searched for in each article can be divided into two large groups. The independent variable of each trial was the post-PCI antiplatelet regimen, of different durations between articles, and different clinical endpoints as dependent variables, mainly intra or post antiplatelet therapy, according to the follow-up time carried out in each study.



PRISMA 2020 flow diagram for new systematic reviews which included searches of databases and registers only

Results

In the search carried out, a total of 533 results were obtained, decreasing to 399 after discarding 134 duplicate articles. According to the abstract reading, 393 articles were eliminated and according to the full text reading, 2 articles were eliminated, one because its main endpoint was to compare groups that used BMS versus DES, and the other because the DAPT used by the experimental group was 1 to 2 months. Therefore, for the purposes of this review, a total of 4 articles were selected for analysis and further discussion.

The selected articles together with their general characteristics were summarized in Table 1. Table 2 presents methodological aspects of the corresponding clinical trials.

Article	Study Name	Author	Magazine	Year	Summary
Ticagrelor plus aspirin for 1 month, followed by ticagrelor monotherapy for 23 months vs aspirin plus clopidogrel or ticagrelor for 12 months, followed by aspirin monotherapy for 12 months after implantation of a drug-eluting stent: a multicentre, open-label, randomized superiority trial.	Global leaders	Vranckx Hotels P. *et al.*	Lancet	2018	Randomized, open label, multicenter It seeks to corroborate hypotheses that 1-month PTSD is superior to 12-month PTSD post-PCI patients (acute and chronic causes), preserving ischemic protection and reducing hemorrhagic events.
Effect of 1-Month Dual Antiplatelet Therapy Followed by Clopidogrel vs 12-Month Dual Antiplatelet Therapy on Cardiovascular and Bleeding Events in Patients Receiving PCI: The STOPDAPT-2 Randomized Clinical Trial	STOPDAPT-2	Watanabe, H. et al.	JAMA	2019	Randomized, open label, multicenter. It seeks to corroborate hypotheses of non-inferiority between 1-month DAPT compared to standard 12-month DAPT in post-PCI patients (acute and chronic causes) in terms of ischemic and hemorrhagic events.
1-Month Dual-Antiplatelet Therapy Followed by Aspirin Monotherapy After Polymer-Free Drug-Coated Stent Implantation	1 Month DAPT	Hong SJ. *et al.*	JACC	2021	Randomized, open label, multicenter. Corroborates hypothesis of non-inferiority of DAPT 1 month (PCI; PF-DCS) vs DAPT 6-12 months (PCI; BP-DES) in post-PCI (acute and chronic causes) and clinical outcomes) patients ischemic/hemorrhagic.
Dual Antiplatelet Therapy after PCI in Patients at High Bleeding Risk	Master DAPT	Valgimigli M. *et al.*	NEJM	2021	Randomized, open label, multicenter. DAPT 1 month vs 6 months post PCI (acute and chronic causes) in patients at high risk of bleeding, seeking to establish non-inferiority in global adverse events and cardiac/cerebral events, and superiority in clinically relevant major or minor hemorrhagic events.

DAPT: Dual Antiplatelet Therapy, PCI: Percutaneous coronary intervention, PF-DCS: Polymer free - Drug-coated stent, BP-DES: Biopolymer - Drug-eluting stent.

Table 1. General characteristics of selected articles

Study Name	Number of patients	SCA vs SCC % clinical presentation	Intervention groups	Endpoints primarios	Tracking
Global Leaders	15968	SCA: 46.8% CCS: 53.2%	1-month DAPT, followed by ticagrelor versus 12-month DAPT.	1st: Death, Q wave myocardial infarction.	24 months
STOPDAPT-2	3045	SCA 38% CCS 62%	1-month PTSD followed by clopidogrel monotherapy versus 12-month DAPT followed by aspirin monotherapy	Cardiovascular death, AMI, hemorrhagic or ischemic stroke, stent thrombosis, minor or major bleeding	12 months
One Month DAPT	3020	SCA 39% CCS 61%	1-month DAPT followed by aspirin monotherapy versus DAPT 6-12 months followed by aspirin monotherapy	Cardiac Death Compound, AMI, culprit vessel revascularization, stroke, major bleeding within 12 months post PCI.	12 months
MASTER DAPT	4434	SCA 47% CCS 53%	1-month DAPT versus DAPT up to 6 months in patients at high bleeding risk	Global adverse clinical events, major cardiac or cerebral events, clinically relevant major or minor haemorrhage	335 days

ACS: Acute Coronary Syndrome, CCS: Chronic Coronary Syndrome, DAPT: Dual Antiplatelet Therapy, AMI: Acute Myocardial Infarction, PCI: Percutaneous Coronary Intervention

Table 2. Relevant methodological aspects of the included clinical trials.

Global Leaders

The GLOBAL LEADERS study included a total of 15,968 study participants, 7,992 were assigned to the experimental group (1-month DAPT), of which 12 withdrew from the study, leaving a total of 7,980; 7,999 patients were assigned to the control group (12 months of DAPT), 11 of whom withdrew, leaving a total of 7,988 in this group. The study was completed by 5,810 patients from the experimental group and 6,981 belonging to the control group, totaling 12,791 patients. The stent used in the coronary intervention was a Biolimus A9-eluting stent (biodegradable polymer-based). The experimental group was administered ticagrelor 90 mg twice daily, plus aspirin 75-100 mg once daily, followed by ticagrelor monotherapy for 23 months. On the other hand, the control group used ticagrelor 90 mg twice a day or clopidogrel 75 mg once a day for 12 months + aspirin 75-100 mg once a day, followed by aspirin monotherapy for 12 months. The primary endpoint evaluated mortality from any cause and incidence of myocardial infarction (associated with a new Q wave on the electrocardiogram). 304 patients in the experimental group died or myocardial infarction was identified versus 349 patients in the control group (RR 0.87 [95% CI 0.75-1.01]; p=0.073). Of the 498 patients who suffered a myocardial infarction, 186 did not die, that is, 37%. Regarding the outcomes of the primary endpoint,

the study concluded that there were no differences between the two schemes. The secondary endpoint consisted of reporting bleeding according to the Bleeding Academic Research Consortium (BARC) criteria, revealing that grade 3 or 5 bleeding occurred in 163 patients (2.04%) in the experimental group versus 169 in the control group (2.12%). %) (RR 0.97 [95% CI 0.78-1.20]; p=0.77). Therefore, the study concluded that 1-month DAPT with ticagrelor + aspirin is not superior to standard 12-month DAPT with clopidogrel or ticagrelor + aspirin. (7) The detail of the incidence of the different events is shown in Table 3.

	GLOBAL LEADERS		STOPDAPT-2		MASTER DAPT		One Month DAPT	
DAPT Months	1 (n=7980)	12 (n=7988)	1 (n=1500)	12 (n=1509)	1 (n=2295)	≤6 (n=2284)	1 (n=1507)	6-12 (n=1513)
Death from any cause	224 (2.8)	253 (3.17)	21 (1.42)	18 (1.21)	-	-	13 (0.9)	20 (1.3)
Death by cause cardiovascular	-	-	9 (0.61)	11 (0.74)	36(1.7)	43(2.0)	6 (0.4) *	10 (0.7) *
AMI	248 (3.11)	250 (3.13)	13(0.88)	11 (0.75)	59(2.7)	46(2.1)	17 (1.1)	22(1.5)
Stent thrombosis	64 (0.80)	64 (0.80)	2 (0.13)	1(0.07)	14(0.6)	8(0.4)	11(0.7)	12(0.8)
Ischemic CVA	63 (0.79)	68 (0.85)	8 (0.54)	15 (1.03)	10(0.5)	17(0.8)	9	5
Hemorrhagic CVA	13 (0.16)	9 (0.11)	0	1 (0.07)	1(<0.1)	4(0.2)	4	11
Haemorrhage								
BARC type 3 to 5	163 (2.04)	169 (2.12)	8 (0.54)	27 (1.81)	49(2.3)	54(2.5)	26 (1.7)	38(2.5)
BARC type 3	150 (1.88)	159 (1.99)	7(0.47)	24 (1.61)	-	-	-	-
BARC type 5	22 (0.28)	24 (0.30)	1 (0.07)	3 (0.20)	2(0.1)	7(0.3)	-	-
TIMI major	-	-	3 (0.20)	16 (1.07)	23(1.1)	24(1.1)	-	-
TIMI minor	-	-	3 (0.20)	7(0.47)	15(0.7)	20(0.9)	-	-
GUSTO moderate to severe	-	-	6 (0.40)	23 (1.54)	44(2.0)	46(2.1)	-	-
SEVERE GUSTO	-	-	4 (0.27)	11(0.74)	8(0.4)	12(0.6)	-	-
GUSTO moderate	-	-	2(0.14)	12(0.80)	36(1.7)	35(1.6)	-	-

DAPT: Dual Antiplatelet Therapy, AMI: Acute Myocardial Infarction, CVA: Cerebrovascular, BARC: Bleeding Academic Research Consortium Criteria, TIMI: Thrombolysis in myocardial infarction bleeding criterio, GUSTO: Global Use of Streptokinase and t-PA for Occluded Coronary Arteries criteria. In terms of "Cardiac Death"

Table 3. Complications per month

STOPDAPT-2

In the STOP DAPT-2 clinical trial, 3045 patients were randomized and 36 withdrew consent. Of the 3,009 patients who did not withdraw consent, 2,974 completed the study, 1,500 being part of the experimental group (1-month DAPT post-PCI) and 1,509 in the control group (12-month DAPT post-PCI). A cobalt-chromium everolimus-eluting stent (CoCr-EES; Cobalt-chromium everolimus-eluting stent) was used in PCI. The DAPT scheme used in the 1-month group was aspirin 81 to 200 mg/day and clopidogrel 75 mg/day or prasugrel 3.75 mg/day, according to the treating physician's criteria. In patients who received prasugrel, this was changed to clopidogrel after a month in both groups. Patients in the experimental group discontinued aspirin after one month and received clopidogrel monotherapy (indicated for 5 years), while the control group received DAPT for 12 months, followed by aspirin monotherapy (indicated for 5 years). 1-month DAPT met the criteria of non-inferiority (p= <0.001) and superiority (p=0.04) versus 12-month DAPT regarding to the primary endpoints shown in Table 2, which occurred in 2.36% and 3.70 % of patients respectively (HR 0.64 [95% CI 0.42-0.98]). Major secondary cardiovascular endpoints (cardiovascular (CV) death, acute myocardial infarction (AMI), stent thrombosis, ischemic and hemorrhagic cerebrovascular attack (CVA)) occurred in 1.96% in 1-month DAPT and 2.51% in 12-month DAPT months, meeting non-inferiority criteria of 1-month DAPT (p= 0.005), but without meeting superiority criteria (p= 0.34) (HR 0.79 [95% CI 0.49-1.29]). Bleeding, considered a secondary major endpoint, occurred in 0.41% of patients with 1-month DAPT, and in 1.54% in 12-month DAPT, meeting superiority criteria in the experimental group (p =0.004). (HR 0.26 [95% CI 0.11-0.64]). (8) The detail of the incidence of the different events is shown in Table 3.

One Month DAPT

The One Month DAPT study enrolled 3,020 patients, of whom 1,507 were assigned to 1-month DAPT and 1,507 assigned to receive 6-12 months of DAPT, both post-angioplasty; randomization occurred prior to this intervention. Those who received 1 month of DAPT followed by aspirin monotherapy were implanted with a Biolimus A9 polymer-free drug-coated stent (PF-DCS; Polymer free drug-coated stent) while those who followed the protocol were followed for 6-12 months. Aspirin monotherapy was implanted with a biodegradable drug-eluting polymer stent (BP-DES; Biopolymer drug eluting stent), either Biolimus A9 or sirolimus with CoCr platform according to operator preference. Aspirin 300 mg + clopidogrel 300 mg were administered at least 12 hours before the intervention in all patients. DAPT consisted of aspirin 100 mg + clopidogrel 75 mg daily post PCI for

1 month or up to 6-12 months depending on the subgroup. The primary endpoint was to assess the occurrences of cardiac death, non-fatal MI, target vessel revascularization, stroke, or major hemorrhage within 12 months post PCI. This endpoint occurred in 88 patients (5.9%) in the abbreviated group and in 98 patients (6.5%) in the group 6-12 months after stent implantation, with DAPT of 1 month not less than the standard therapy (p= <0.001), but without achieving superiority criteria (p = 0.475) (HR 0.90; 95% CI 0.68-1.20). As a secondary endpoint, the occurrence of coronary stent thrombosis was evaluated, occurring in 11 patients (0.7%) in the 1-month DAPT group and in 12 patients (0.8%) in the 6-12-month DAPT group (HR 0.90; 95% CI 0.41-2.09; p=0.842 for superiority criteria). There was major bleeding in 26 patients (1.7%) in the experimental group and 36 patients (2.5%) in the control group (HR 0.69; 95% CI 0.42-1.13; p = 0.136 for superiority criteria). (9) The detail of the incidence of the different events is shown in Table 3.

Master DAPT

The Master DAPT study included 4,579 patients randomized 30 to 40 days post-PCI, free of ischemic and hemorrhagic events, who adhered to DAPT, of whom 4,434 completed the protocol. The patients were divided into subgroups, with 2,295 designated for abbreviated therapy and 2,284 for standard therapy. A sirolimus-eluting biodegradable polymer stent was implanted in the PCI. The choice of the drug P2Y12 for DAPT and the type of post-DAPT monotherapy was at the investigator's discretion, with clopidogrel being the most frequently used. In the population that completed the protocol, global adverse clinical events (death from any cause, AMI, stroke, major bleeding) occurred in 165 patients (7.5%) on abbreviated therapy and 172 (7.7%) on standard therapy, meeting non-inferiority criteria (p<0.001) (HR 0.97; 95% CI 0.78-1.20). In the same population, 133 patients (6.1%) on abbreviated therapy and 132 (5.9%) on standard therapy had a major cardiac or cerebral event (HR 1.02; 95% CI 0.80-1.30; p= 0.001 for non-inferiority). In the intent-to-treat population (n=4579), the incidence of major bleeding or clinically relevant bleeding was lower among patients on abbreviated therapy (6.5%) than in patients on standard therapy (9.4%) who met the criteria for superiority (p<0.001) (HR 0.68; 95% CI, 0.55-0.84). (10) The detail of the incidence of the different events is shown in Table 3.

Discussion

PCI is a frequently used alternative in the treatment of coronary disease, characterized in recent years by the use of DES, lipid-lowering drugs that modulate atherothrombotic risk, and a change in the profile of patients in terms of greater non-cardiac morbidity and mortality. DAPT has turned out to be a fundamental piece in the prevention of post-implantation ischemic complications of the coronary device, such as stent thrombosis, being supported being supported by different clinical trials, within which the following studies ares cited as elementary pillars: ISAR (11), STARS (12), FANTASTIC (13), AND MATTIS (14), (15,16).

Both the technological development of coronary stents and the paradigm shift in the patient profile have presented a new problem regarding the bleeding risk of patients with an indication for DAPT, taking into account that bleeding events represent a component of high morbidity and mortality. since the evidence indicates that the impact of a major hemorrhagic event is equal to or greater than a myocardial infarction in terms of mortality. (6) Despite the evolution of coronary devices, with DES currently being superior to BMS, the optimal duration of DAPT continues to be a subject of constant debate that has given rise to numerous clinical trials comparing shortened and standard duration regimens. (15) There are few clinical trials that adopt and analyze ultra-short 1-month DAPT schemes, which could represent a more efficient approach in terms of non-inferiority/superiority in the prevention of bleeding complications with respect to standard therapy, always considering the prevention of ischemic complications as a fundamental aspect.

GLOBAL LEADERS is characterized for being the 1-month clinical trial using DAPT with the largest number of participants and having a low rate of discontinuation of experimental therapy compared to other large studies. The results of this study do not support a change in the duration of DAPT, since the study failed to demonstrate the superiority of abbreviated therapy, concluding that 1-month DAPT with ticagrelor + aspirin is not superior to standard 12-month DAPT. with clopidogrel or ticagrelor + aspirin. The non-superiority of 1-month DAPT is reflected in the results of the endpoints of the study. Regarding the primary endpoint, there was no greater numerical difference between groups when analyzing the number of patients who suffered a myocardial infarction and/or died, on the other hand, in the secondary endpoint, nor was the difference statistically significant in terms of hemorrhagic events. It is important to highlight that this clinical trial was not designed to assess the non-inferiority of 1-month DAPT compared to standard DAPT, so this aspect cannot be analyzed, unlike the other 3 studies reviewed. The study has the particularity of continuing with ticagrelor monotherapy instead of aspirin, which is the most classic. Thanks to this, the study was very useful to strengthen the evidence

related to the efficacy and safety of ticagrelor monotherapy. It is relevant to mention that due to the use of this drug, differences may be found in its results, compared to studies in which aspirin monotherapy is used. Within the limitations of GLOBAL LEADERS, it is worth noting that the occurrence of the primary endpoint in the control group, analyzed at 2 years, was lower than expected, possibly due to the use of ticagrelor instead of clopidogrel, consistent with the results obtained in the PLATO study, which somewhat limits the weight of the results. (17) Another limitation was that some electrocardiograms could not be analyzed, in a proportion of 5%, which is very high.

In STOPDAPT-2, patients on the 1-month DAPT regimen followed by clopidogrel monotherapy, compared with 12 months of DAPT, resulted in a significantly lower rate of cardiovascular and bleeding events, meeting non-inferiority and superiority criteria for the mentioned. Most of the patients were of low or intermediate ischemic risk, very few of high ischemic risk. In patients with very high ischemic risk, the requirement for intensive antithrombotic therapy post-PCI has been postulated; however, in the analysis of this subgroup in STOPDAPT-2, there was no statistically significant difference between patients with a regimen of 1 versus 12 months of DAPT with regarding the appearance of ischemic events, therefore the duration of DAPT of 1 month may be an option in them. (18) It should be considered that since it is only a subgroup, which is directly affected by the reduction in DAPT time, specific studies with a high number of participants are necessary to be able to conclude correctly on the effectiveness of the DAPT change. Furthermore, this study was conducted exclusively in patients who received CoCr-EES in their PCI, therefore it is unknown whether the results of the present study can be extrapolated to other currently used DES. The findings of this clinical study suggest that a shorter duration of DAPT may provide benefits, reducing bleeding events without increasing cardiovascular events during the post-PCI period studied, although additional research in other populations is needed given the limitations of the study.

One Month DAPT reveals that one month of DAPT followed by aspirin monotherapy in patients implanted with PF-DCS stents is non-inferior to 6-12 months of DAPT followed by aspirin monotherapy in patients implanted with BP-DES stents, in events such as myocardial infarction' heart failure, cardiac death, target vessel revascularization, and stroke. Some limitations associated with the trial should be considered, such as the difference between the stents used between both study groups, and even within the same DAPT 6-12 month group; however, in the latter, there were no major differences regarding outcomes between those treated with Biolimus A9 and Sirolimus. On the other hand, it is a study that was conducted in a population with low bleeding risk, so it is not possible to infer these results in higher risk populations. Also, there was no specific duration of DAPT in the 6-12 group, leading to statistical bias given the inhomogeneous duration among patients in this group.

Studies included in this systematic review, GLOBAL LEADERS and STOP DAPT-2, are cited by the authors of One Month DAPT when using the 1-month DAPT strategy, emphasizing the discontinuation of aspirin after one month of DAPT in the mentioned studies, where they proceed with the use of other antiplatelet drugs in monotherapy, because One Month DAPT uses aspirin as monotherapy after DAPT, which raises different study designs and therefore other possible results despite the same duration of therapy.

The MASTER DAPT tonic reveals that the discontinuation of DAPT in a median of 34 days post PCI is not inferior to its continuation in a median of 193 days in relation to adverse clinical events (Table 2) and major cardiac or cerebral events, and higher for clinically relevant major or minor bleeding, where in the intent-to-treat population, there was a decrease of at least 3% in abbreviated DAPT. The selection of the population at high bleeding risk stands out in this study, which contrasts with the population selected in GLOBAL LEADERS and STOP DAPT 2. Unlike the other studies included in this review, it is important to emphasize the randomization that occurred 30-44 days after PCI, which allowed the use of inclusion criteria in this period of time, increasing the precision in the selection of patients with high bleeding risk. There are limitations that should be emphasized, such as the heterogeneous duration of DAPT in patients in the standard therapy group, due to the discontinuation of therapy by some patients. MASTER DAPT shows superiority of abbreviated DAPT in patients with high bleeding risk in an objective manner, which could certainly be extrapolated given the nature of these patients.

The studies included in this review used DES of different generations and models. The fact that each of the reviewed clinical trials have used limited DES models raises the question of whether the results of the 1-month DAPT groups are also possible to obtain with other DES, due to the lack of studies that cover the theme of superiority of DAPT between DES of the same generation and between different generations.

Within the systematic search carried out, two studies were also analyzed that were not included in this review for reasons previously explained. The STOPDAPT-2 ACS study randomized 4169 patients and compared 1- or 2-month DAPT vs. standard DAPT (12 months) in terms of ischemic and hemorrhagic events, in post-PCI patients exclusively for ACS. DAPT of 1 or 2 months did not meet non-inferiority criteria (P=0.06) with respect to 12 months of DAPT, since hemorrhagic events decreased in the experimental group, but ischemic events increased, therefore, these results do not support recommending 1 month DAPT over standard therapy. (21) The SENIOR study used 1-month DAPT schedules for patients with ACS; and 6 months for CCS, with 1200 patients being randomized. This

study was not designed to evaluate the optimal duration of DAPT, since the purpose of this study was to compare results between BMS and DES, in the context of abbreviated DAPT, where it was sought to compare major cardiac or cerebrovascular adverse events between the groups; One of their conclusions is that DES is better than BMS in the use of DAPT for 1-6 months, having good results in terms of ischemic and hemorrhagic events in both groups, which supports the safety of abbreviated therapy, both in BMS and in DES. (22)

Conclusion

This systematic review provides evidence of the non-inferiority of 1-month DAPT compared to standard post-PCI DAPT in patients with both acute and chronic coronary disease, in relation to adverse clinical event outcomes; however, further studies are needed to determine the superiority of it. Research is necessary in populations at high ischemic and hemorrhagic risk, due to the great implication of reducing the time of DAPT in them.

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