Efficacy and safety of short-term (≤ 6 months) duration of dual antiplatelet therapy after drug-eluting stents: a meta-analysis of randomized controlled trials

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Abstract

Objective: Optimal duration of dual antiplatelet therapy (DAPT) after drug-eluting stent (DES) implantation remains controversial. The present study is an assessment of efficacy and safety of short-term (≤6 months) DAPT after DES implantation in patients with coronary artery disease, especially in important subgroups.

Methods: PubMed, Embase, and the Cochrane Central Register of Controlled Trials were searched for randomized, controlled trials comparing short-term and long-term (>6 months) DAPT after DES implantation. Primary efficacy outcome was stent thrombosis (ST). Primary safety outcome was major bleeding. Pooled relative risks (RRs) with 95% confidence interval (CI) were calculated using random- or fixed-effects models as appropriate.

Results: Total of 7 trials involving 15870 patients were included in the study. Short-term DAPT significantly reduced major bleeding by 49% compared with long-term DAPT (RR: 0.51; 95% CI: 0.32–0.80; p=0.003) without increasing risk of ST (RR: 1.28; 95% CI: 0.83–1.97; p=0.266). In addition, no differences were observed in all-cause mortality, myocardial infarction (MI), cardiac mortality, or cerebrovascular accidents. Moreover, no significant difference in composite of cardiovascular events, bleeding, and mortality was found in important clinical subgroups.

Conclusion: Short-term DAPT is associated with lower bleeding risk compared with long-term DAPT. Number of ST and MI was higher with short-term DAPT without reaching statistical significance. Comprehensive clinical judgment is necessary to weigh benefits and risks in the individual patient. *(Anatol J Cardiol 2017; 17: 168-75)*

Keywords: antiplatelet therapy, coronary artery disease, drug-eluting stent

Introduction

Dual antiplatelet therapy (DAPT) is the cornerstone for patients undergoing percutaneous coronary intervention (PCI) and can effectively reduce risk of stent thrombosis (ST) and ischemic events (1–3). This comes, however, at the expense of an increased risk of bleeding. To balance efficacy and safety of DAPT, the American Heart Association and American College of Cardiology guidelines recommend at least 12 months of DAPT after drug-eluting stent (DES) implantation (4, 5). This is based on support from observational and surveillance studies of first-generation DES. Subsequently, the European Society of Cardiology guidelines recommended 6 months of DAPT following implantation of second-generation or newer DES for stable coronary artery disease (6). Yet optimal duration of DAPT after DES implantation remains controversial.

Recently, 3 large, randomized, controlled trials [DAPT (7), ISAR-SAFE (8), and ITALIC (9)] have examined benefits and risks of DAPT treatment for up to 6 months or beyond 1 year. However, results were seemingly conflicting or heterogenous. DAPT trial revealed extended DAPT significantly reduced risks of ST and major adverse cardiovascular and cerebrovascular events (MACCE), but was associated with increased risk of bleeding (7). In ITALIC trial, 6-month duration of DAPT showed similar benefit and risks of bleeding and thrombotic events compared with 24-month DAPT (9). Furthermore, recent results from ISAR-SAFE trial indicated that net clinical benefit of short-term and long-term DAPT (L-DAPT) was similar (8).

Several previous meta-analyses have assessed efficacy and safety of short-term DAPT (S-DAPT) after DES implantation

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Accepted Date: 03.10.2016 **Available Online Date:** 10.11.2016

DOI:10.14744/AnatolJCardiol.2016.7285

(10–13); however, we noticed that statistical evaluations were all performed at population level. It is opinion of present study authors that since every individual has different risk of bleeding and ST, enhancing precision in assessment of S-DAPT in important subgroups is more important than statistical approach performed at an overall level. Therefore, we sought to identify relative benefits and risks of S-DAPT in key clinical subgroups and offer clinicians a more comprehensive picture of S-DAPT based on current research evidence.

Methods

Data sources and search strategy

Records of PubMed, Embase, and the Cochrane Central Register of Controlled Trials databases dating from inception to September 2015 were comprehensively and systematically searched without language restriction. Search was limited to randomized controlled trials (RCTs) that compared S-DAPT to L-DAPT after DES implantation. Search terms included "drug eluting stent" and "dual antiplatelet." In order to acquire additional potentially eligible trials, reference lists of articles chosen for inclusion and recent reviews were manually screened.

Study selection and eligibility criteria

The following inclusion criteria were applied in PICOS order: (1) population: patients received DAPT after DES implantation; (2) intervention and comparison: duration of DAPT≤6 months versus >6 months. DAPTs used were aspirin and clopidogrel; (3) availability of complete clinical data; and (4) study design, RCT.

Data extraction and quality assessment

Two independent reviewers (CL Xiang and LJ Zeng) performed data abstraction. Discrepancies were resolved through discussion between the 2 investigators. For each study, first author, year of publication, sample size, population characteristics, stent type, duration of follow-up, and outcome data were recorded. Primary efficacy outcome was ST. ST was defined as definite or probable ST according to the Academic Research Consortium classification (14). Primary safety outcome was major bleeding, based on one of the following definitions: 1) TIMI, Thrombolysis in Myocardial Infarction; 2) REPLACE-2, Randomized Evaluation of PCI Linking Angiomax to Reduced Clinical Events; 3) GUSTO, Global Utilization of Streptokinase and Tissue Plasminogen Activator for Occluded Arteries; or 4) BARC, Bleeding Academic Research Consortium (15) (Table 1). Secondary outcomes of interest were all-cause mortality, myocardial infarction (MI), cardiac mortality, cerebrovascular accidents. Cochrane Collaboration's tool was used to assess methodological quality of selected RCTs (16). Two investigators (CL Xiang and LJ Zeng) reviewed all studies and assigned a value of "low," "high," or "unclear" to the following domains: random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, and selective reporting or other bias (16).

Statistical analysis

Relative risk (RR) with 95% confidence intervals (CI) for dichotomous outcomes was calculated. I2 statistic was used to test heterogeneity between studies. I2 statistic of <25%, 25% to 50%, and >50% indicated low heterogeneity, moderate heterogeneity, and high heterogeneity, respectively (17). Outcomes were then pooled and compared with fixed-effects models (I2<50%) or random-effects models (I2≥50%) (17–19). P value <0.05 was considered statistically significant. All statistical analyses were performed using STATA software, version 12.0 (Stata Corp., College Station, TX, USA).

According to implanted stent type, sensitivity analysis was performed to detect heterogeneity or investigate possible influence of use of different type of stent in some clinical trials (20).

Pre-specified subgroup analysis was also performed to assess relative benefit and risks of S-DAPT in important clinical subgroups: age (years <65 or ≥65 years), sex, history of diabetes, renal function (creatinine clearance ≤60 mL/min or >60 mL/min), left ventricular ejection fraction (LVEF) (<50% or ≥50%), acute coronary syndrome (ACS)/unstable coronary disease, bifurcation, multi-stent, simple or complex lesion(s). Pooled RRs were calculated using inverse variance method.

Results

Literature search and study characteristics

Study selection process is illustrated in Figure 1 (21). Initial search yielded 2342 relevant publications, from which 2335 were excluded due to duplicate studies or other reasons (non-RCT, review, editorial, study design, ongoing trails, or no original data). Finally, 7 RCTs with total of 15870 participants were included in this meta-analysis (8, 9, 22–26). Major characteristics (duration of DAPT, stent type, follow-up, percentage of male participants and those with diabetes, hypertension, or dyslipidemia) of the 7 RCTs included are presented in Table 1. Trials were published between 2012 and 2015. Sample size ranged from 1399 to 4000. Average age of the patients was similar between trials, while median follow-up period for outcome evaluation was of significant difference (range: 1–3 years). Majority of stents used in included trials were second-generation DES (proportion >86%; Table 1). Composite of cardiovascular events, bleeding, and mortality was evaluated as primary outcome in all trials.

Quality assessment of selected RCTs is provided in Figure 2 in the supplemental material. Although most of the studies were open-label, randomized trials, blinded adverse events adjudication was implemented. As adverse events are clearly defined and blinded outcome adjudication was implemented, it was decided that open-label design was not significant source of bias. Publication bias was not assessed because pooled estimate included fewer than 10 trials (27).

Table 1. Characteristics of included randomized studies

	Gwon et al., 2012 (EXCELLENT) (22)		Valgimigli et al., 2012 (PRODIGY) (24)		Kim et al., 2012 (RESET) (23)		Feres et al., 2013 (OPTIMIZE) (25)		Gilard et al., 2015 (ITALIC) (9)		Colombo et al., 2014 (SECURITY) (26)		Schulz-Schüpke et al., 2015 (ISAR-SAFE) (8)	
	S-DAPT	L-DAPT	S-DAPT	L-DAPT	S-DAPT	L-DAPT	S-DAPT	L-DAPT	S-DAPT	L-DAPT	S-DAPT	L-DAPT	S-DAPT	L-DAPT
Duration, months	6	12	6	24	3	12	3	12	6	12	6	12	6	12
Patients, n	722	721	983	987	1059	1058	1563	1556	912	910	682	717	1997	2003
Age, years mean*	63.0±9.6	62.4±10.4	67.9±11	67.8±11	62.4±9.4	62.4±9.8	61.3±10.4	61.9±10.6	61.7±10.9	61.5±11.1	64.9±10.2	65.5±10.1	67.2 (59.3–73.3)	67.2 (59.1–73.7)
Male gender	65%	64%	76%	77%	64%	63%	64%	63%	81%	79%	78%	77%	81%	81%
Diabetes	38%	39%	24%	25%	30%	29%	35%	35%	36%	38%	30%	31%	25%	24%
Hypertension	73%	74%	70%	73%	62%	61%	86%	88%	65%	65%	75%	71%	90%	92%
Dyslipidemia	75%	76%	53%	56%	58%	60%	63%	64%	67%	67%	65%	61%	88%	87%
Stent type														
BMS	0%	0%	25%	25%	0%	0%	0%	0%	0%	0%	0%	0%	0.4%	0.3%
1st-gen. DES	25%	25%	25%	25%	0%	28%	0%	0%	0%	0%	0%	0%	11%	10%
2nd-gen. DES	75%	75%	50%	50%	100%	72%	100%	100%	100%	100%	100%	100%	88%	89%
Follow-up (months)	12	12	24	24	12	12	12	12	36	36	24	24	15	15
MB criteria	TIMI	TIMI	TIMI	TIMI	TIMI	TIMI	REPLACE-2, GUSTO	REPLACE-2, GUSTO	TIMI	TIMI	BARC	BARC	TIMI	TIMI
Primary Endpoint	Composite of cardiac death, MI, or TVR during 1-year period after randomization.		Incidence of death from any cause, nonfatal MI, or cerebrovascular accident at 2 years		Composite of cardiovascular death, MI, ST, TVR, or bleeding at 1 year		Composite of death from any cause MI, stroke, or MB at 1 year		Composite of death, MI, emergency TVR, stroke, or MB within 12 months after stenting		Composite of cardiac death, MI, stroke, ST, or type 3 or 5 bleeding at 12 months		Composite of death MI, ST, stroke, or MB at 9 months after randomization	

*Age data of ISAR-SAFE are shown as median (interquartile range). BARC - Bleeding Academic Research Consortium; BMS - bare metal stent; DAPT - dual antiplatelet therapy; DES - drug-eluting stent; GUSTO - Global Utilization of Streptokinase and Tissue Plasminogen Activator for Occluded Arteries; L-DAPT - long-term (>6 months) duration of DAPT after drug-eluting stent; MB - major bleeding; MI - myocardial infarction; PCI - percutaneous coronary intervention; REPLACE-2 - Randomized Evaluation of PCI Linking Angiomax to Reduced Clinical Events; S-DAPT - short-term (≤6 months) duration of DAPT after drug-eluting stent; ST - stent thrombosis; TIMI - thrombolysis in myocardial infarction; TVR - target vessel revascularization

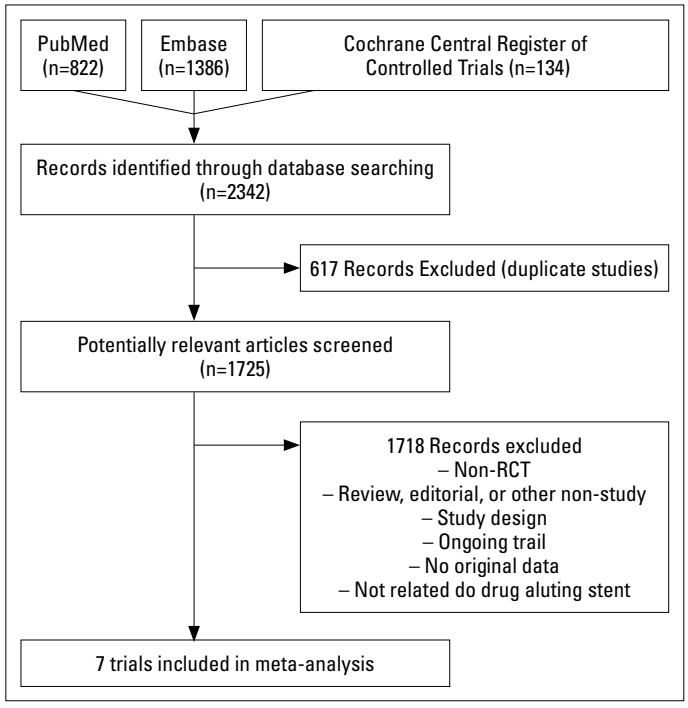

Figure 1. Flow diagram of literature search. RCT - randomized controlled trial

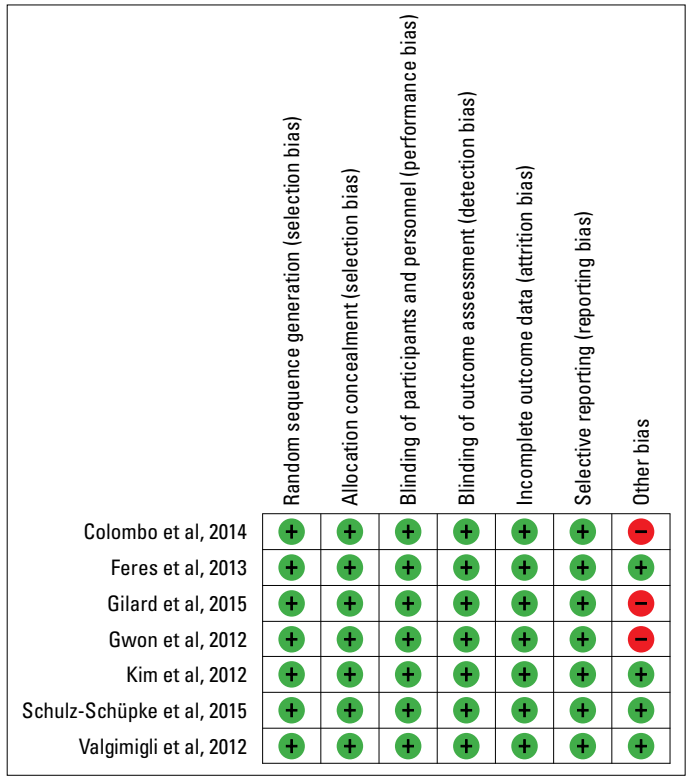

Figure 2. Assessment of quality of selected RCTs. Low risk of bias (green circles), unclear risk of bias (yellow circles), and high risk of bias (red circles). Other Bias is due to problems not covered elsewhere in the table. Criteria for judgment of "Low risk" of bias: Study appears to be free of sources of bias. Criteria for judgment of "High risk" of bias: There is at least 1 important risk of bias. For example, study had a potential source of bias related to specific study design used, or has been claimed to be fraudulent, or had some other problem. Criteria for judgment of "Unclear risk" of bias: There may be risk of bias, but there is either insufficient information to assess whether important risk of bias exists, or insufficient rationale or evidence that identified problem will introduce bias

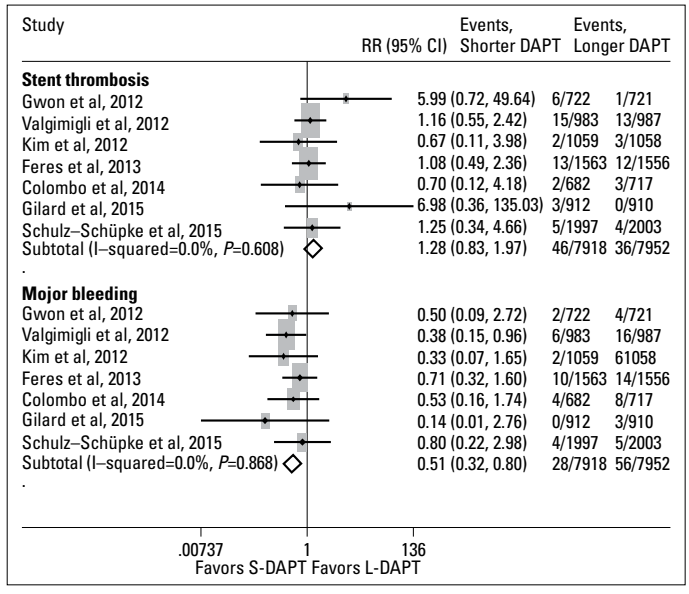

Figure 3. Forest plot for primary outcomes: stent thrombosis and major bleeding. DAPT - dual antiplatelet therapy; L-DAPT - duration of DAPT >6 months; S-DAPT - duration of DAPT ≤6 months. Outcomes were pooled and compared with fixed-effects models

Primary outcomes

ST

All RCTs reported ST (8, 9, 22–26). Outcomes of ST were pooled and compared with fixed-effects model (Fig. 3). There was no significant difference in ST according to duration of S-DAPT and L-DAPT (RR: 1.28; 95% CI: 0.83–1.97; p=0.266), and there was low heterogeneity among studies (I2=0.0%; p=0.608). Sensitivity analysis excluding trials containing bare metal stent (BMS) or including only trials containing second-generation DES did not appreciably alter findings (Table 2).

Major bleeding

All RCTs reported major bleeding (8, 9, 22–26). Outcomes of major bleeding were pooled and compared with fixed-effects model (Fig. 3). Risk of major bleeding was significantly reduced in S-DAPT when compared with control group (RR: 0.51; 95% CI: 0.32–0.80; p=0.003), and there was low heterogeneity among studies (I2=0.0%; p=0.868). Sensitivity analysis excluding trials containing BMS did not appreciably alter findings (RR: 0.53; 95% CI: 0.30–0.92; p=0.024) (Table 2). Major bleeding did not differ between short and long DAPT when only trials containing second-generation DES were analyzed (RR: 0.58; 95% CI: 0.30–1.09; p=0.092) (Table 2).

Secondary outcomes

All-cause mortality

All RCTs reported all-cause mortality (8, 9, 22–26). Outcomes of all-cause mortality were pooled and compared with fixed-effects model (Fig. 4). No significant difference in all-cause

Table 2. Sensitivity analysis according to type of stent implanted

	Stent thrombosis	Major bleeding	All-cause mortality	Myocardial infarction	Cardiac mortality	Cerebrovascular accidents
Excluding trials with BMS	(RR: 1.36; 95% CI: 0.76-2.44; *P*=0.299)	(RR: 0.53; 95% CI: 0.30-0.92; *P*=0.024)	(RR: 0.91; 95% CI: 0.66-1.26; *P*=0.564)	(RR: 1.20; 95% CI: 0.88-1.64; *P*=0.242)	(RR: 0.96; 95% CI: 0.63-1.45; *P*=0.834)	(RR: 0.92; 95% CI: 0.51-1.66; *P*=0.773)
Excluding trials with BMS and first-generation DES	(RR: 1.20; 95% CI: 0.61-2.35; *P*=0.598)	(RR: 0.58; 95% CI: 0.30-1.09; ***P=0.092***)	(RR: 0.99; 95% CI: 0.69-1.41; *P*=0.940)	(RR: 1.17; 95% CI: 0.84-1.65; *P*=0.352)	(RR: 1.03; 95% CI: 0.66-1.60; *P*=0.904)	(RR: 1.02; 95% CI: 0.45-2.29; *P*=0.971)

Outcomes were pooled and compared with fixed-effects models. BMS - bare metal stent; CI - confidence interval; DES - drug-eluting stent; RR - relative risk

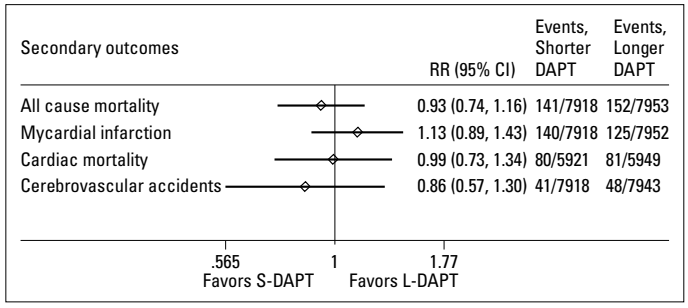

Figure 4. Forest plot for secondary efficacy and safety outcomes. Data are n/N. Heterogeneity: all-cause mortality I2=0.0%, P=0.914; myocardial infarction I2=0.0%, P=0.859; cardiac mortality I2=0.0%, P=0.835; cerebrovascular accidents I2=1.0%, P=0.417. DAPT - dual antiplatelet therapy; L-DAPT - duration of DAPT >6 months; S-DAPT - duration of DAPT ≤6 months. Outcomes were pooled and compared with fixed-effects models

mortality was found between experimental group and control group (RR: 0.93; 95% CI: 0.74–1.16; p=0.530), and there was low heterogeneity among studies (I2=0.0%; p=0.914). Sensitivity analysis excluding trials containing BMS or including only trials containing second-generation DES did not appreciably alter findings (Table 2).

Myocardial infarction

All RCTs reported MI (8, 9, 22–26). Outcomes of MI were pooled and compared with fixed-effects model (Fig. 4). Risk of MI was similar in comparison of S-DAPT and L-DAPT (RR: 1.13; 95% CI: 0.89–1.43; p=0.327), and there was low heterogeneity among studies (I2=0.0%, p=0.859). Sensitivity analysis excluding trials containing BMS or including only trials containing second-generation DES did not appreciably alter findings (Table 2).

Cardiac mortality

Six RCTs reported cardiac mortality (9, 22–26). Outcomes of cardiac mortality were pooled and compared with fixed-effects model (Fig. 4). There was no significant difference seen in cardiac mortality between S-DAPT and L-DAPT (RR: 0.99; 95% CI: 0.73–1.34; p=0.949), with low heterogeneity among studies (I2=0.0%; p=0.835). Sensitivity analysis excluding trials containing BMS or including only trials containing second-generation DES did not appreciably alter findings (Table 2).

Cerebrovascular accidents

All RCTs reported cerebrovascular accidents (8, 9, 22–26).

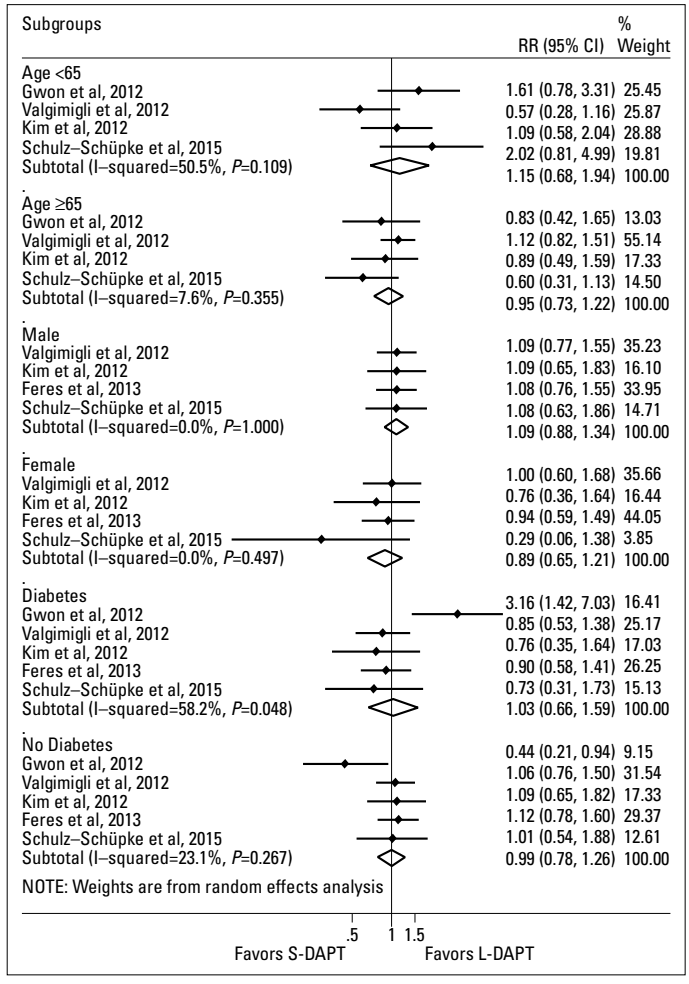

Figure 5. Forest plot for composite of cardiovascular events, bleeding, and mortality in important clinical subgroups. Data available from Schulz-Schüpke et al., 2015, for age was years <67.2 or ≥67.2 years. DAPT - dual antiplatelet therapy; L-DAPT - duration of DAPT >6 months; S-DAPT - duration of DAPT ≤6 months. Pooled relative risks (RRs) were calculated using inverse variance method

Outcomes of cerebrovascular accidents were pooled and compared with fixed-effects model (Fig. 4). No significant difference was observed in cerebrovascular accidents in comparison of S-DAPT and L-DAPT (RR: 0.86; 95% CI: 0.57–1.30; p=0.472), and there was low heterogeneity among studies (I2=1.0%; p=0.417). Sensitivity analysis excluding trials containing BMS or including only trials containing second-generation DES did not appreciably alter findings (Table 2).

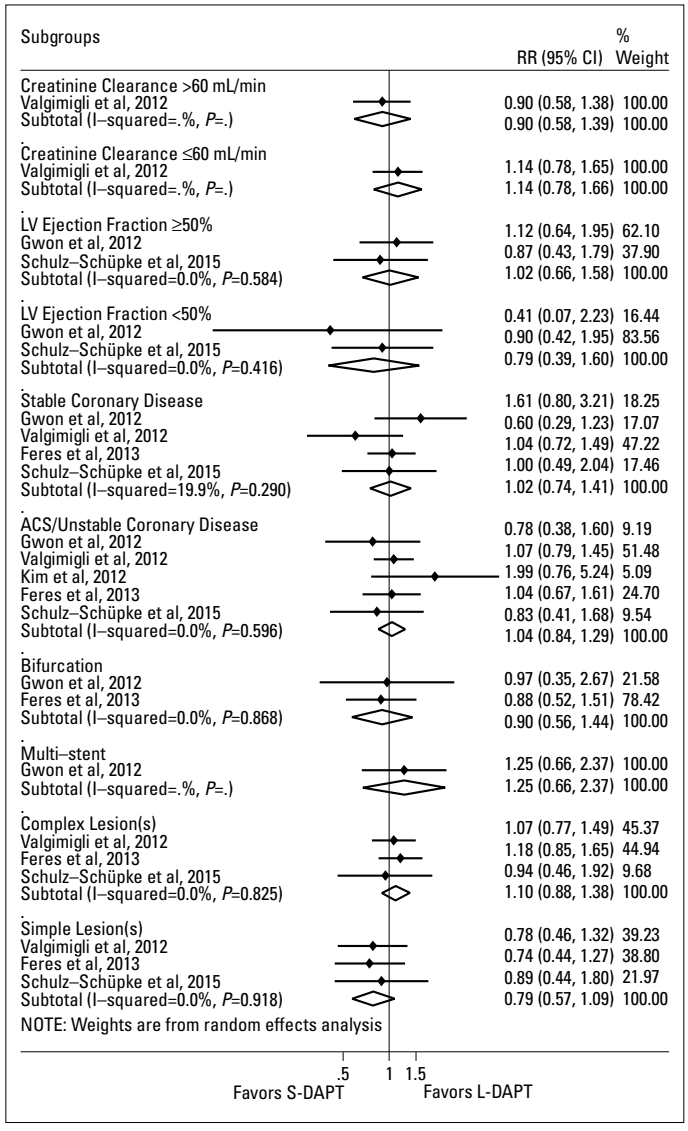

Figure 6. Forest plot for composite of cardiovascular events, bleeding, and mortality in important clinical subgroups. Data available from Schulz-Schüpke et al., 2015, for left ventricular ejection fraction was ejection fraction <55% or ≥55%. ACS - acute coronary syndrome; DAPT - dual antiplatelet therapy; L-DAPT - duration of DAPT >6 months; LV - left ventricular; S-DAPT - duration of DAPT ≤6 months. Pooled relative risks (RRs) were calculated using inverse variance method

Composite of cardiovascular events, bleeding, and mortality in important clinical subgroups

Analysis of pre-specified subgroup was conducted to assess relative benefits and risks of S-DAPT in important clinical subgroups (Fig. 5, 6). No significant difference in composite of cardiovascular events, bleeding, and mortality was found between S-DAPT and L-DAPT for subgroups of age (year <65 or ≥65 years), sex, history of diabetes, renal function (creatinine clearance ≤60 mL/min or >60 mL/min), LVEF (<50% or ≥50%), ACS/unstable coronary disease, bifurcation, multi-stent, simple or complex lesion(s).

Discussion

The present study is meta-analysis of 7 large RCTs to evaluate efficacy and safety of S-DAPT for patients undergoing PCI. Results demonstrate that S-DAPT significantly reduced major bleeding by 49% compared with L-DAPT (RR: 0.51; 95% CI: 0.32–0.80; p=0.003) without increasing risk of ST (RR: 1.28; 95% CI: 0.83–1.97; p=0.266). On the other hand, S-DAPT was non-inferior to L-DAPT in reducing risk of all-cause mortality, MI, cardiac mortality, or cerebrovascular accidents. Sensitivity analysis showed that data from a few patients treated with BMS or first-generation DES did not appreciably alter findings. Results of this meta-analysis are robust.

However, current meta-analysis differs from current guidelines' recommendation of 6 to 12 months. This can be explained by the following factors. It's worth noting that currently recommended duration of DAPT is based on observational and surveillance studies of first-generation DES. In contrast, majority of stent types used in current RCTs included in this meta-analysis were second-generation DES (Table 1). Strong evidence has demonstrated that second-generation DES are safer with lower ST risk compared with first-generation DES (28). They were also associated with reduction in target vessel MI and target lesion revascularization (29).

Since every individual has different risk of bleeding and ST, enhancing precision in assessment of S-DAPT in important subgroups is more important than statistical approach performed at overall level. For example, bleeding risk is driven by elderly age (≥75 years), history of bleeding (e.g., gastrointestinal), history of stroke or TIA, low body weight, or disease of liver or kidney (30). Patients with ACS, lesion complexity, diabetes, hypertension, or dyslipidemia have increased risk of ST (30). These patients are often underrepresented in trials. For this reason, relative benefits and risks of S-DAPT in important clinical subgroups were investigated. Our subgroup analysis didn't demonstrate any impact due to age (<65 or ≥65 years), sex, history of diabetes, renal function (creatinine clearance ≤60 mL/min or >60 mL/min), LVEF (<50% or ≥50%), ACS/unstable coronary disease, bifurcation, multi-stent, simple or complex lesion(s) on composite of cardiovascular events, bleeding, and mortality. These results may benefit from improved biocompatibility and decreased thrombogenicity. Previous evidence reveals that second-generation DES has significant risk reduction in late and very late ST compared with earlier-generation DES (31, 32). However, caution should be used before generalizing subgroup analysis results for individual patients for several reasons. First, definitions of composite primary endpoint of included trials were heterogeneous, which may affect statistical power of the evidence. At the same time, we have also taken note that due to lack of patient-level data of each component of composite events (e.g., ST and MI), subgroup analysis was based on composite events of cardiovascular events, bleeding, and mortality. Therefore, though there was no

significant difference seen in risk of composite events between S-DAPT and L-DAPT, risk of ST and MI of key subgroup under DAPT treatment for up to 6 months remains uncertain. More evidence is needed to clarify benefits of S-DAPT with respect to ST and MI. Nonetheless, these subgroup analysis findings do provide clinical reference for individualized DAPT management.

Present meta-analysis supports recent findings of studies reporting that S-DAPT significantly reduced major bleeding events without increasing risk of ST, all-cause mortality, MI, cardiac mortality, or cerebrovascular accidents (8, 9, 22–26, 33, 34). While L-DAPT effectively reduced risk of ST and ischemic events, risk of bleeding increases with longer duration of treatment. Thus, maintaining balance between efficacy and safety for optimal DAPT duration for patients undergoing PCI is the key point. Although a recent study found that CHA2DS2-VASc and HAS-BLED scores have some reference value for MACCEs and prediction regarding major bleeding after stent placement, there is currently still no gold standard for evaluation of ischemic and bleeding risk after PCI (35–37).

As a clinician, comprehensive clinical judgment is necessary to weigh benefits and risks in the individual patient based on risk factors for bleeding and ST after DES placement. Present study results provide evidence supporting S-DAPT for patients with low risk of ischemic events or high risk of bleeding. S-DAPT should be considered in those patients to increase clinical benefit. But what is the solution for patients with DES who are at high risk of ST or MI and low risk of bleeding? In this study, we found that S-DAPT tended to increase risk of ST and MI (combined RRs >1; Fig. 3, 4), though this trend was not statistically significant. In addition, since these high-risk patients were not represented in clinical studies, application of S-DAPT is not recommended for these patients. Studies of evidence-based medicine have demonstrated that extended DAPT (e.g. 30 months) could significantly reduce risk of ST, but this effect was significantly attenuated with use of second-generation DES and was accompanied by increased risk of bleeding (38). Extended DAPT duration should be considered for patients such as those with ACS, lesion complexity, diabetes, hypertension, or dyslipidemia.

Study limitations

The main limitations of present study are related to the following aspects. First, due to lack of patient-level data of each component of composite events, subgroup analysis was based on composite events of cardiovascular events, bleeding, and mortality. Although no significant difference in composite events was found in important clinical subgroups, risk of ST or major bleeding of key subgroup undergoing DAPT treatment for up to 6 months remains uncertain. Of the 3 trials containing 100% second-generation DES, only study of Feres et al. (25), in which short DAPT was defined as ≤3 months, was included in subgroup analysis, given lack of adequate data. Secondly, multiple types of stents were tested in individual trials. Although the majority of stents used in the included trials were second-generation DES, early stents were still used in about 13% of cases (BMS: 3.2%; first-generation DES: 9.9%). Sensitivity analysis can help mitigate potential effect of heterogeneity on validity of the results.

Conclusions

S-DAPT is associated with lower bleeding risk compared with L-DAPT. Instances of ST and MI were numerically higher with S-DAPT, yet without reaching statistical significance. Comprehensive clinical judgment is necessary to weigh benefits and risks for individual patient. S-DAPT is most likely to be of benefit for patients who are at high risk of bleeding but who are also at low risk for ischemic events.

Funding sources: None.

Conflict of interest: None declared.

Peer-review: Externally peer-reviewed.

Authorship contributions: Concept – C.L.X., Y.H.; Design – C.L.X., Y.Z.G.; Supervision – Y.H.; Funding – C.L.X., Y.H.; Materials – C.L.X., L.J.Z.; Data collection &/or processing – C.L.X., L.Z.; Analysis and/or interpretation – C.L.X., Y.Z.G.; Literature review – C.L.X., B.B.L.; Writing – C.L.X., Y.Z.G., L.J.Z.; Critical review – Y.H.

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