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Combo CD34-Antibody Covered Sirolimus-Eluting Coronary Stent Versus Standard Drug-Eluting Stents: A Meta-analysis on Efficacy and Safety Outcomes

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Research Article

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Abstract

Background: The combo dual therapy stent, a sirolimus-eluting stent with CD34 antibodies, has proposed advantages over the standard drug-eluting stents (DES).

Methods: A meta-analysis was performed of all randomized controlled trials (RCT) to compare Combo versus standard DES.

Results: A total of five RCTs were included with 4,391 patients and a median-weighted follow-up of 1.27 years. Standard DES was favored in the outcomes of target lesion failure (TLF) (Combo 7.3% vs Standard 4.6%, p=0.001), target lesion revascuarlization (TLR) (Combo 4.0% vs Standard 2.2%, p=0.004), and target vessel revascuarlization (TVR) (Combo 5.9% vs Standard 3.4%, p=0.0006). Similar results were seen for studies with one year follow up: TLF (Combo 6.4% vs Standard 3.8%, p=0.0004), TLR (Combo 3.5% vs Standard 1.8%, p=0.19), and (Combo 5.3% vs Standard 3.1%, p=0.0009). However, the effects were not seen after two years. Moreover, these effects were seen to be rooted in the studies that included the standard sirolimus-eluting stents: TLF (Combo 6.7% vs Standard 4.2%, p=0.005), TLR (Combo 3.7% vs Standard 1.8%, p=0.0008), and TVR (Combo 5.3% vs Standard 3.0%, p=0.0006). There was no difference in cardiac death, target vessel myocardial infarction, target vessel failure, and stent thrombosis.

Conclusion: The combo stent has higher rates of TLF, TLR, and TVR, which is possibly due to increased endothelialization, stent material, and unsustainable benefits. These effects were specifically attributed to the standard sirolimus-eluting stent.

Keywords: Combo, sirolimus, drug-eluting, meta-analysis, prospective, efficacy, safety.

Introduction:

In the modern-day United States, coronary artery disease (CAD) is the primary cause of morbidity and mortality. Unstable atherosclerosis plaques in the coronary arteries have been treated with percutaneous coronary intervention for many decades now [1]. The stents have advanced from a bare-metal stent with a stainless steel wire mesh structure to drug-eluting stents (DES) to overcome or minimize numerous challenges, such as neointimal response and angioplasty restenosis [2]. First-generation DES consist of sirolimus and paclitaxel; whereas, second-generation

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DES are everolimus, zotarolimus, and biolimus. Even though the efficacy and safety of the second-generation DES have markedly improved over the last decade, very late stent thrombosis, in-stent stenosis, and in-stent neoatherosclerosis have been noticed [3,4].

To overcome these issues, the research community has trialed a novel method of a 'pro-healing' approach where endothelial progenitor cell (EPC) capturing stents accelerate re-endothelialization within 72 hours [5,6]. Therefore, the GenousTM stent (OrbusNeich Medical, Fort Lauderdale, Florida) was produced, which is a bare-metal stent with anti-CD34 antibodies coating to capture EPCs [7]. A single-arm meta-analysis of patients with CAD who received the Genous stents demonstrated an alarmingly high rate of failure and adverse outcomes at follow-up of one year [8]. Thereafter, a similar stent was made, but with CD34+ antibodies on the abluminal surface of a sirolimus drug-eluting stent (SES) and is called ComboTM dual therapy stent (OrbusNeich Medical, Fort Lauderdale, Florida). Animal studies have shown benefits with the combo stent. In an observational study by Ellenbroek et al, 12 white rabbits received both a combo stent and an everolimus-eluting stent. They found that at 28 days the combo stent had significantly higher endothelialization by histology and neointimal hyperplasia by optical coherence tomography (OCT) [9]. Furthermore, Lee et al published an observational study of human subjects with combo stent placement and OCT that demonstrated that combo stents have neointimal regression, minimal restenosis, and no stent thrombosis at 24-36 months. Therefore, these stents are proposed to prevent early late complications of incomplete endothelial coverage while maintaining anti-restenotic effectiveness [10]. This meta-analysis was conducted to confirm this theory by pooling prospective studies that compared combo stents versus any standard DES in patients with coronary artery disease who received a coronary stent. The standard DES are defined as either first-generation or second-generation DESs that are not coated with any other substance.

Materials and Methods:

We conducted a comprehensive search of the electronic databases of PUBMED, EMBASE, and COCHRANE from inception to August 2021 for relevant studies. The inclusion criteria consisted of: (1) a prospective double-arm study, either randomized controlled trial (RCT) (2) compared combo CD34 antibody-covered SES versus standard DES, (3) standard DES were either sirolimus, everolimus, paclitaxel, zotarolimus, or biolimus DESs that are not coated with any other substance, (4) reported either efficacy or safety outcomes, and (5) human subjects. Exclusion criteria were the following: (1) ongoing or irretrievable data, (2) single-arm study, (3) retrospective study, (4) use of bare-metal stents, (5) use of Genous dual-therapy stent, (6) use of animals, and (7) no clinical outcome endpoint. This meta-analysis was performed in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines.

The search included the following keywords: "CD34", "combo", "sirolimus", "randomized trial", "prospective", "efficacy", "safety", "mortality", "coronary artery disease", "CAD". Two authors (RMP and ZQB) independently reviewed the search results, extracted potential articles, and assessed their eligibility. The Cochrane Collaboration risk-of-bias tool was used by two different authors (RMP and ZQB) to assess the quality of the included studies.

The primary outcome of this meta-analysis was target lesion failure (TLF), which was defined as the composite endpoint of cardiac death or all-cause mortality, target lesion revascularization (TLR), and target vessel myocardial infarction (TV-MI). Secondary outcomes included cardiac death, TLR, TV-MI, target vessel failure (TVF), target vessel revascularization (TVR), and stent thrombosis. Stent thrombosis was defined as definite and probable thrombosis as per the Academic Research Consortium-2 [11]. For each outcome, two subgroup analyses were performed to analyze the effect of study design and follow-up duration. If the statistics favored the standard DES, an additional subgroup analysis was conducted to evaluate the types of standard DES. We also collected baseline characteristics of the included studies and patients.

Statistical analysis was conducted using Review Manager (RevMan), version 5.4 (The Cochrane Collaboration, Copenhagen, Denmark). The Mantel-Haenszel random-effects models were used to estimate the risk ratios (RR) and the corresponding 95% confidence intervals (CI). Two-sided p values of <0.05 were considered statistically significant. I2 statistics were used to assess statistical heterogeneity.

Results

Five RCTs were included with a total of 4,391 patients and a median-weighted follow-up of 1.27 years (Figure 1) [12,13,14,15,16]. The characteristics of the included studies and patients are described in (Tables 1 and 2). The statistical values of RRs, 95% CIs, and p-values are illustrated in Table 3 and the pertinent ones are included below.

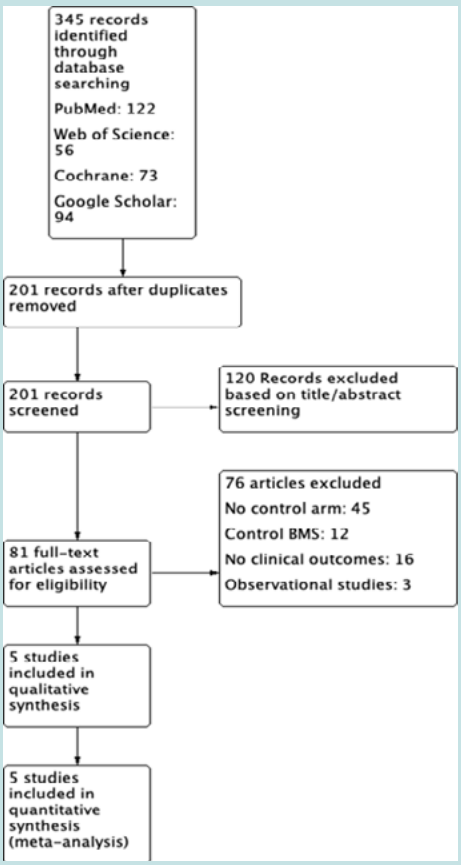


Figure 1: The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow diagram

Table 1: Characteristics of included studies

Study name	First author	Publication year	Study design	Study population	Patients (n)	Type of Combo	Type of Standard DES	Latest follow-up (y)
REMEDEE-OCT[12]	Jaguszewski et al	2017	RCT, Multicenter	ACS, de novo CAD lesion with diameter 2.5-3.5 mm and length less than 20 mm, or diameter stenosis 50-100%, undergoing PCI with stent	58	Combo SES (OrbusNeich, Ft Lauderdale, FL)	Xience V CoCr-EES (Abbott Vascular, Santa Clara, CA)	1.5
HARMONEE[13]	Saito et al	2018	RCT, Multicenter	Older than 19 years, de novo CAD lesion with diameter 2.5-3.5 mm and length less than 20 mm, or diameter stenosis 50-100%, undergoing PCI with stent	572	Combo SES (OrbusNeich, Ft Lauderdale, FL)	Xience V CoCr-EES (Abbott Vascular, Santa Clara, CA)	1
REMEDEE[14]	Haude et al	2019	RCT, Multicenter	Older than 18 and younger than 80 years, de novo CAD lesion with diameter 2.5-3.5 mm and length less than 20 mm	183	Combo SES (OrbusNeich, Ft Lauderdale, FL)	Taxus Liberté	5
RECOVERY[15]	Tao et al	2021	RCT, Multicenter	Older than 18 and younger than 75 years with de novo CAD	432	Combo SES (OrbusNeich, Ft Lauderdale, FL)	Nano polymer-free SES (Lepu Medical Technology, Beijing, China)	5
SORT OUT X[16]	Jakobsen et al	2021	RCT, Multicenter	Older than 18 years and CAD undergoing PCI with stent	3146	Combo SES (OrbusNeich, Ft Lauderdale, FL)	Xience V CoCr-EES (Abbott Vascular, Santa Clara, CA)	1

Legend: ACS, Acute coronary syndrome; CAD, Coronary artery disease; DES, Drug-eluting stent; EES, Everolimus-eluting stent; RCT, Randomized controlled trial; SES, Sirolimus-eluting stent; ZES, Zotarolimus-eluting stent. Values are reported as number of patients or mean ± standard deviation.

Table 2: Baseline characteristics of included patients

Study name	Publication year	Sample size (n)	Age (years)	Males	Smokers (Current or former) (n)	Diabetes mellitus (n)	Hypertension (n)	Dyslipidemia (n)	Previous MI (n)	Previous PCI (n)	Previous CABG (n)	Reference vessel diameter (mm)	Diameter stenosis (%)	Lesion length (mm)
		Combo stent												
		Standard drug-eluting stent												
REMEDEE-OCT[12]	2017	28	62.8 ± 10.7	24	6	4	18	18	2	NR	NR	2.56 (2.13 - 2.83)	6.9 ± 6.9	15.0 (13.51-17.96)
		30	59.4 ± 11.3	21	12	4	17	17	0	NR	NR	2.60 (2.32 - 2.89)	7.1 ± 5.5	15.29 (11.57-17.24)
HARMONEE[13]	2018	287	67.6 ± 9.6	211	191	117	218	225	45	72	4	2.73 ± 0.43	65.49 ± 10.9	16.70 ± 7.10
		285	66.5 ± 10.4	212	175	93	220	227	45	83	5	2.75 ± 0.46	65.11 ± 15.5	14.67 ± 6.33
REMEDEE[14]	2019	124	64.20 ± 9.48	89	71	41	100	102	31	29	4	2.77 ± 0.42	NR	13.69 ± 5.07
		59	64.05 ± 10.49	42	28	22	45	43	16	12	2	2.85 ± 0.34	NR	14.64 ± 4.41
RECOVERY[15]	2021	216	58.3 ± 9.6	147	97	43	116	27	29	21	1	2.89 ± 0.52	67.7 ± 11.6	16.3 ± 7.24
		216	59.3 ± 8.4	137	93	46	130	37	28	20	1	2.89 ± 0.50	68.4 ± 13.4	17.1 ± 7.73
SORT OUT X[16]	2021	1578	67.1 ± 10.7	1213	410	279	835	783	240	295	111	3.4 ± 0.6	NR	22.8 ± 15.6
		1568	66.7 ± 10.9	1208	429	271	871	783	221	303	89	3.4 ± 0.6	NR	22.8 ± 15.8

Legends: CABG, coronary artery bypass grafting; MI, Myocardial infarction; NR, not reported; PCI, Percutaneous coronary intervention.Values are reported as Combo | Standard and number of patients or mean ± standard deviation.

Table 3: Overview of statistical analysis results.

Outcome		Combo rate (%)	Standard rate (%)	RR	95% CI	p-value	I^2 (%)	Summary
TLF	All studies	7.3	4.59	1.5	1.17, 1.90	0.001	0	Significantly favored standard DES
	1 year	6.39	3.82	1.7	1.26, 2.22	0.0004	0	Significantly favored standard DES
	>2 years	12.35	9.82	1.1	0.71, 1.76	0.64	0	No difference
	SES	6.69	4.2	1.6	1.14, 2.14	0.005	11	Significantly favored standard DES
	EES	6.67	4.44	1.5	0.78, 2.98	0.23	0	No difference
	PES	17.74	16.95	1.1	0.53, 2.07	0.9	NA	
CD	RCT	1.3	1.17	1.1	0.66, 1.85	0.71	0	No difference
	1 year	1.43	1.27	1.1	0.65, 1.91	0.7	0	
	>2 years	0.59	0.69	1	0.16, 6.31	1	0	
TLR	RCT	4.03	2.22	1.7	1.18, 2.38	0.004	1	Significantly favored standard DES
	1 year	3.49	1.81	1.9	1.28, 2.91	0.002	0	Significantly favored standard DES
	>2 years	7.06	5.09	1.2	0.65, 2.32	0.53	0	No difference
	SES	3.68	1.79	2	1.35, 3.10	0.0008	0	Significantly favored standard DES
	EES	4.13	3.17	1.3	0.58, 2.99	0.52	0	No difference
	PES	8.87	10.17	0.9	0.34, 2.24	0.78	NA	No difference

TV-MI	RCT	2.64	2.09	1.2	0.76, 1.91	0.44	12	No difference
	1 year	2.54	1.7	1.5	0.96, 2.32	0.08	0	Insignificantly favored standard DES
	>2 years	3.24	4.73	0.7	0.29, 1.55	0.35	0	No difference
TVF	RCT	10.93	7.22	1.3	0.80, 1.95	0.33	0	No difference
	1 year	7.3	5.08	1.4	0.77, 2.68	0.26	0	
	>2 years	20.16	18.64	1.1	0.57, 2.05	0.81	NA	
TVR	RCT	5.91	3.43	1.6	1.24, 2.16	0.0006	0	Significantly favored standard DES
	1 year	5.28	3.08	1.7	1.25, 2.36	0.0009	0	
	>2 years	9.41	5.82	1.4	0.78, 2.48	0.26	0	Insignificantly favored standard DES
	SES	5.3	2.97	1.8	1.28, 2.48	0.0006	0	Significantly favored standard DES
	EES	6.35	4.44	1.4	0.73, 2.81	0.3	0	
	PES	13.71	11.86	1.2	0.51, 2.63	0.73	NA	No difference
ST	RCT	0.45	0.42	0.9	0.31, 2.84	0.91	10	No difference
	1 year	0.53	0.42	1.3	0.50, 3.16	0.63	0	
	>2 years	0	0.36	0.2	0.01, 3.87	0.26	NA	

Legends: CD, cardiac death; CI, confidence interval; EES, everolimus-eluting stent, RCT, randomized controlled trial; RR, risk ratio; NA, not applicable; SES, sirolimus-eluting stent; ST, stent thrombosis; TLF, target lesion failure; TLR, target lesion revascularization; TVR, target vessel revascularization; TVF, target vessel failure; TV-MI, target vessel myocardial infarction; PES, paclitaxel-eluting stent

The primary outcome of TLF significantly favored standard DES in the RCTs (Combo 7.3% vs Standard 4.6%, RR 1.49, 95% CI 1.17-1.90, p=0.001, I^2=0%) (Figure 2). After one year of follow-up, TLF significantly favored standard DES (Combo 6.4% vs Standard 3.8%, RR 1.67, 95% CI 1.26-2.22, p=0.0004, I_2=0%), but there was no difference after two years (Combo 12.35% vs Standard 9.8%, RR 1.12, 95% CI 0.71-1.76, p=0.64, I^2=0%) (Figure 3). When evaluating the types of the standard DES, the patients with SES significantly favored the standard DES (Combo 6.7% vs Standard 4.2%, RR 1.57, 95% CI 1.14-2.14, p=0.005, I^2=11%) (Figure 4).

As described above, TLF is a composite outcome of cardiac death, TLR, and TV-MI. There was no difference in cardiac death between combo and standard DES when analyzed by study design or follow-up duration (Figures 5 and 6). TLR significantly favored the standard DES in RCTs (Combo 4.0% vs Standard 2.2%, RR 1.68,

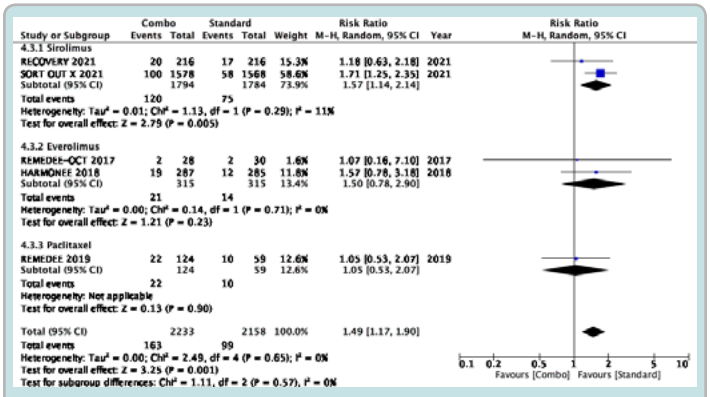


Figure 4: Target lesion failure based on type of standard drug-eluting stent.

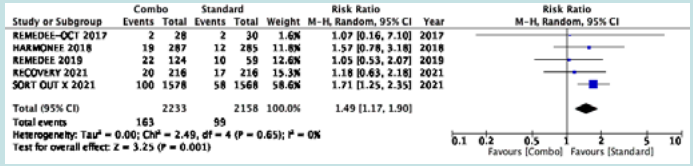


Figure 2: Target lesion failure based on study design.

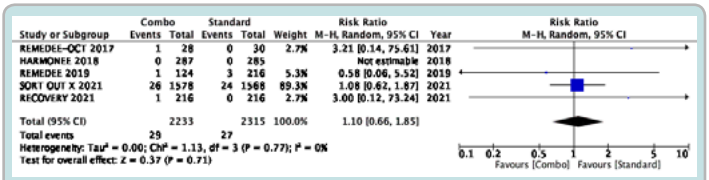


Figure 5: Cardiac death based on study design.

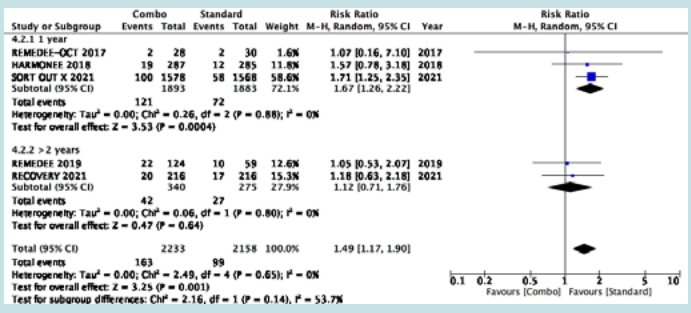


Figure 3: Target lesion failure based on follow-up duration

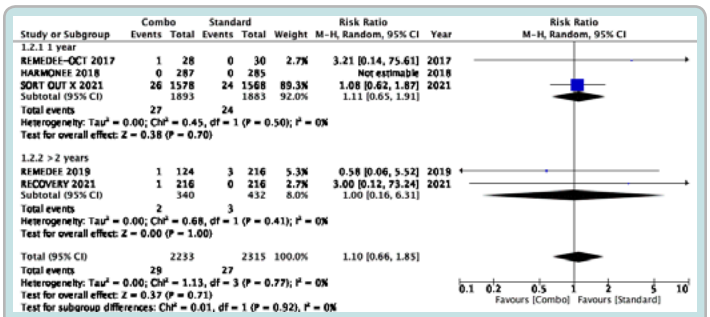


Figure 6: Cardiac death based on follow-up duration

95% CI 1.18-2.38, p=0.004, I^2=1%) and one year follow-up (Combo 3.5% vs Standard 1.8%, RR 1.93, 95% CI 1.28-2.91, p=0.19, I^2=52%) (Figures 7 and 8). However, after two years of follow-up there was no difference (Combo 7.1% vs Standard 5.1%, RR 1.23, 95% CI 0.65-2.32, p=0.53, I^2=0%) (Figure 8). When evaluating the different types of standard DES, we saw that TLR significantly favored the standard DES when SES was used (Combo 3.7% vs Standard 1.8%, RR 2.04, 95% CI 1.35-3.10, p=0.0008, I^2=0%) (Figure 9). Of the studies included, there was no difference in TV-MI between the two arms (Figure 10). TV-MI insignificantly favored the standard DES after one year (Combo 2.5% vs Standard 1.7%, RR 1.49, 95% CI 0.96-2.32, p=0.08, I^2=0%), but there was no difference after two years (Figure 11).

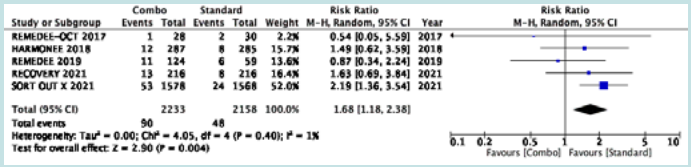


Figure 7: Target lesion revascularization based on study design

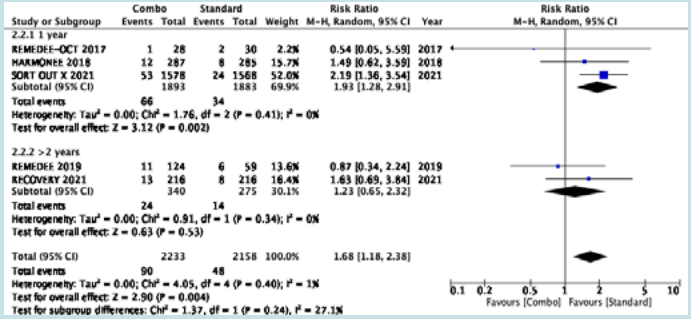


Figure 8: Target lesion revascularization based on follow-up duration

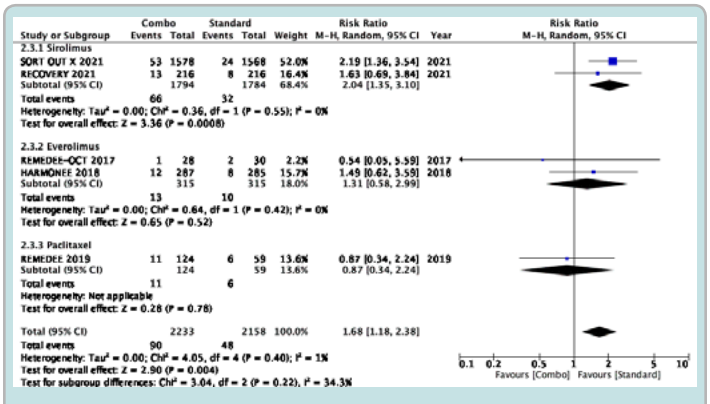


Figure 9: Target lesion revascularization based on type of standard drug-eluting stent

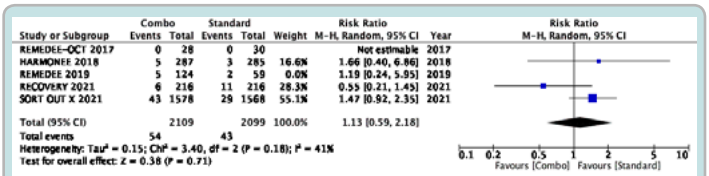


Figure 10: Target vessel myocardial infarction based on study design.

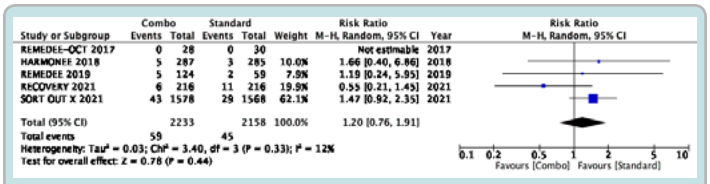


Figure 11: Target vessel myocardial infarction based on follow-up duration.

In regards to TVF, there was no difference between the two arms (Figures 12 and 13). TVR, on the other hand, significantly favored standard DES in RCTs (Combo 5.9% vs Standard 3.4%, RR 1.63, 95% CI 1.24-2.16, p=0.0006, I^2=0%) and one year follow-up (Combo 5.3% vs Standard 3.1%, RR 1.72, 95% CI 1.25-2.36, p=0.0009, I^2=0%). However, when the follow-up was greater than two years TVR insignificantly favored the standard DES (Combo 9.4% vs Standard 5.8%, RR 1.39, 95% CI 0.78-2.48, p=0.26, I^2=0%) (Figures 14 and 15). The SES significantly favored the standard DES arm for the TVR (Combo 5.3% vs Standard 3.0%, RR 1.78, 95% CI 1.28-2.48, p=0.0006, I^2=0%) (Figure 16). Finally, there was no difference in stent thrombosis between combo and standard DES (Figures 17,18 and 19).

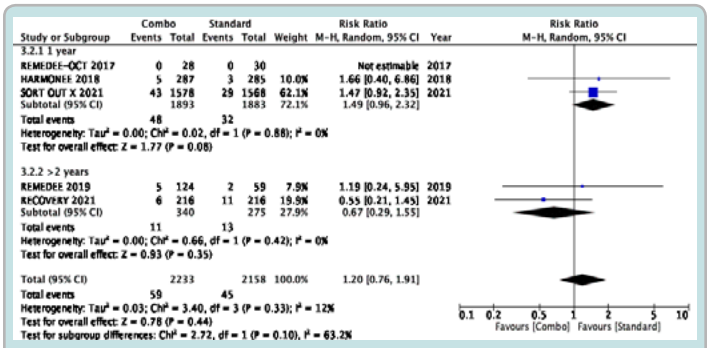


Figure 12: Target vessel failure for randomized controlled trials.

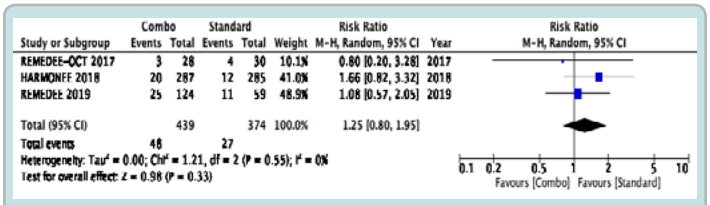


Figure 13: Target vessel failure based on follow-up duration.

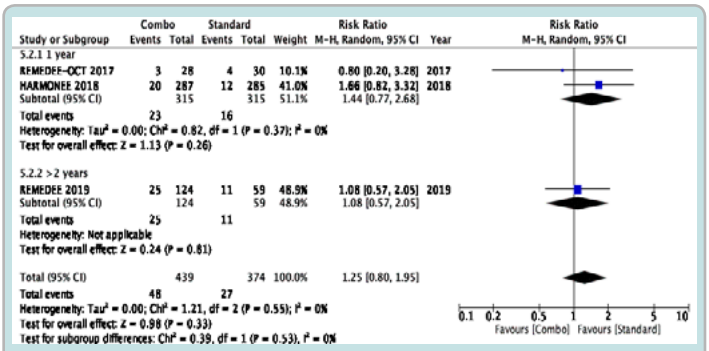


Figure 14: Target vessel revascularization for randomized controlled trials

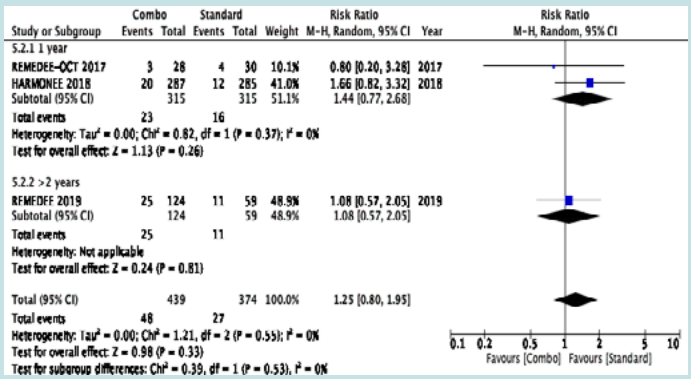


Figure 14: Target vessel revascularization for randomized controlled trials

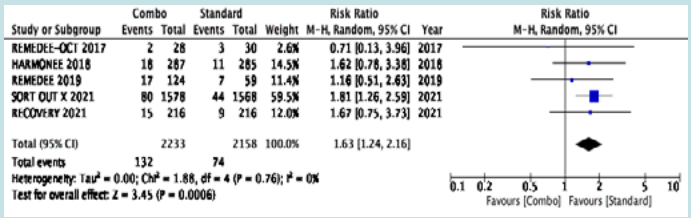


Figure 15: Target vessel revascularization based on follow-up duration

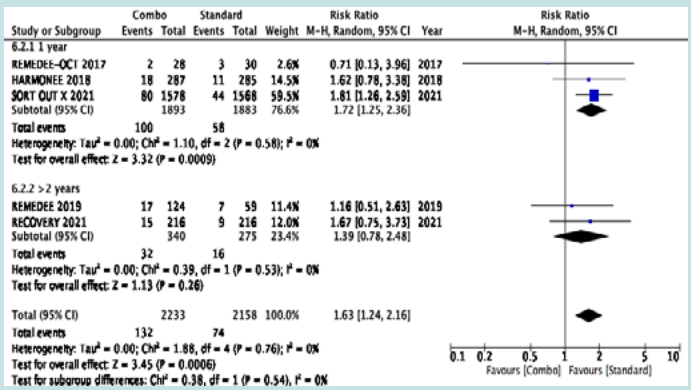


Figure 16: Target vessel revascularization based on type of standard drug-eluting stent

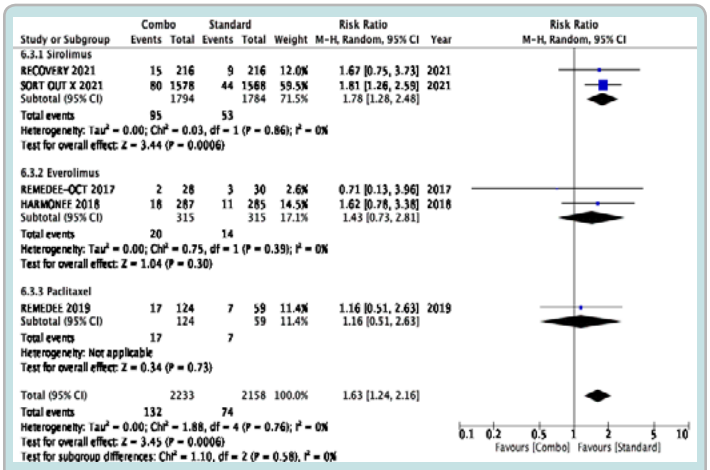


Figure 17: Stent thrombosis (definite and probable) based on study design.

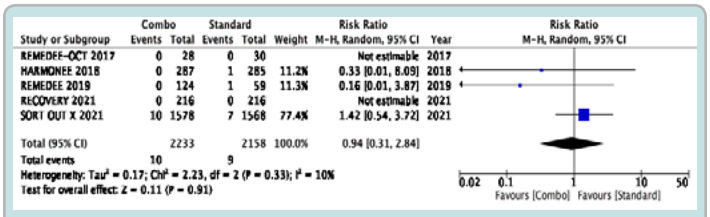
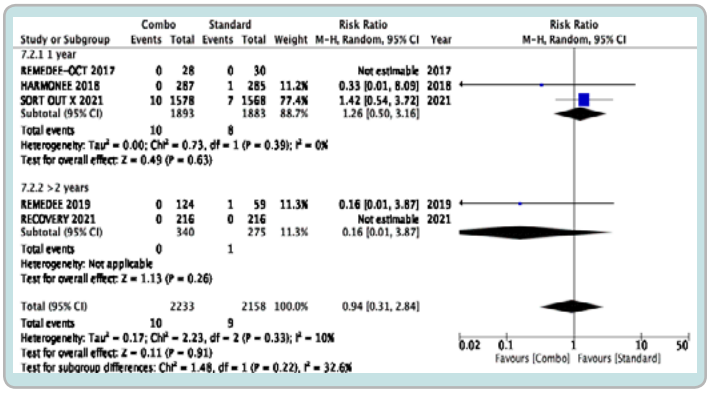


Figure 18: Stent thrombosis (definite and probable) based on follow-up duration



Discussion:

In this meta-analysis, we found that the composite outcome of TLF and individual outcome of TLR significantly favored standard DES in RCTs and after one year of follow-up. Moreover, we found that TLF and TLR effects were both significantly associated with standard SES. There was an insignificantly higher rate of TV-MI in the standard DES. TVR also favored standard DES and was mainly due to the standard SES. Finally, there was no difference in cardiac death, TVF, stent thrombosis between combo and standard DES.

Recently, there have been three RCTs published that have compared combo stents and standard DES. In 2021, the large-scale SORT OUT X RCT was published by Jakobsen et al where a total of 3146 patients received combo or the Xience V SES. After one year, the standard SES had a significantly lower rate of TLR (p=0.0012); however, there was no statistical significance in TLF, all-cause death, cardiac death, myocardial infarction [16]. Two other recent RCTs were published - RECOVERY by Tao et al in 2019 and REMEDEE by Haude et al in 2021 - and demonstrated that there was no difference in clinical or safety outcomes at two and five years, respectively, between combo and standard DES [14,15].

Our meta-analysis confirms the results of the included RCTs that the standard DES is more efficient and safe for patients with CAD who are receiving a coronary stent. These favorable differences were significantly seen in TLF and TLR. TLR is known as clinically indicated percutaneous or surgical revascularization of the index lesion during follow-up [17]. We propose the theory that this effect of TLF and TLR is multifaceted by: an over-increased level of early endothelialization, stent material difference, and unsustainable short-term benefits in the mid- and long-term setting. As described before, the CD34 antibodies in the combo stent promote early endothelialization by allowing CD34+ cells and vascular endothelial growth factors to induce therapeutic angiogenesis in myocardial ischemia of animals [18,19]. However, a recent retrospective study by Blessing et al showed that in

patients with OCT-guided revascularization by combo stents there was a 40% rate of restenosis and 60% rate of neointimal formation at a median follow-up of 189 days [20]. Although there was no difference in the incidence of stent thrombosis in the included total cohort, it might be important to demonstrate the rates of stent thrombosis and TV-MI in particular subsets, such as ACS and diabetes. Another mechanism for worse outcomes is the diffuse process of endothelialization instead of focally near the infarcted vessel and lesion.

The combo stents also have significant differences in their material from the standard DES. In regards to the combo stent, the strut thickness is 100 micrometers, drug-eluting only lasts 30-45 days, and absorption time only lasts 90 days. On the other hand, the three standard DES in this meta-analysis (Xience, Orsiro, and Taxus) have a smaller strut thickness of 60-90 micrometers, drug elution time is prolonged at over 120 days, and absorption time is either 15 months or permanent [21]. Therefore, the disadvantages with combo stents are not with the drug-eluting component, but rather the CD34 antibodies and different materials. Additionally, focal myocardial ischemia and subsequent regional angiogenesis cause ischemia in the epicardial coronary vessels that are proximal to the ischemic focus. Thus, a larger collateral system may alleviate the ischemia, but not by the increased microcirculation from the CD34 antibodies in the combo stent.(Nagy, Schaper, Jargon [22,23,24].

TVR includes restenosis, disease progression, and stent thrombosis [25]. The results from this meta-analysis indicate that there was a significant benefit in TVR for the standard DES, but there was no difference in-stent thrombosis. Therefore, we propose that the significant difference seen in the TVR outcome is mainly attributed to disease progression, as was depicted in a previous prospective observational study [25].

Our meta-analysis also demonstrated that not only did the outcomes favor standard DES, but they were specifically linked to the standard SES. Sirolimus, a first-generation standard DES, has powerful immunosuppressive activity by inhibiting protein synthesis as well as cell cycle progression and migration [26]. Paclitaxel is a similar medication, but is less effective and has a smaller therapeutic index [27]. Additionally, everolimus is a second-generation standard DES; however, it has a shorter half-life and a quicker onset of endothelialization [28,29]. Therefore, in accordance with our meta-analysis the first generation standard SES should be preferentially used over paclitaxel and the second generation standard SES.

Retrospective studies on animals and humans have reported beneficial outcomes with the combo stent, but had a short-term follow-up duration of 28 days and 24-36 months, respectively [9,10]. Our meta-analysis with a follow-up period of 1.27 years demonstrated that the standard DES had beneficial clinical outcomes of TLF, TLR, and TVR at one year, but there was no difference in the studies with greater than two years of follow-up. Due to the differences between combo stents and standard DES as described above, it is apparent that the short-term benefits of DES do not last long.

There are limitations to this meta-analysis, including a limited number of trials with a median-weighted follow-up period of only 1.27 years, despite including two five-year studies. The included studies differed in the definition of TLF, as some included cardiac mortality and others included all-cause mortality. Although we delineated first-generation and second-generation DES without additional coating materials as 'standard DES', there is no such defined group in the literature. The trials also used different types of standard SES for the control group. A subgroup analysis was performed to compare these different types in specific outcomes. Additionally, there are no current studies comparing the combo stent versus a placebo or medical management arm. A meta-regression analysis was unable to be performed with the existing data, as the data were reported at a study level and not at a patient level. Since the DES is known to have increased mortality, we are unable to differentiate the cardiac death rates seen in the combo arm. We propose that medications should be evaluated in these patients to treat the systemic atherosclerotic process. Thus, RCTs should be conducted to compare patients with combo stents who receive dual antiplatelet therapy, such as the REDUCE trial by De Luca et al [30]. The studies also did not indicate whether the included patients had ST elevated myocardial infarctions or non-ST elevated myocardial infarctions at presentation. We propose further RCTs to confirm that the beneficial effects are not seen after two years. Additionally, the association between TV-MI and standard DES needs to be further defined. Specific RCTs should be conducted to compare standard SES versus the other standard DES. Finally, previous studies have indicated that alcohol consumption and smoking cessation can lead to an increased rate of endothelization, which may confound our proposal [31,32].

Conclusion:

This updated meta-analysis demonstrates that the combo stent was associated with poorer clinical and safety outcomes, as compared to the standard DES. Our hypothesis for these findings with the combo stent is: over-increased level of early endothelialization, stent material difference, and unsustainable short-term benefits in the mid- and long-term setting. Therefore, the standard DES should remain the mainstay choice for a stent in patients with CAD.

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None

Conflicts of Interest:

The authors report no relationships that could be construed as a conflict of interest.

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