ORIGINAL RESEARCH ARTICLE

Cardiovascular Therapeutics

The Role of Vascular Imaging in Guiding Routine Percutaneous Coronary Interventions: A Meta-Analysis of Bare Metal Stent and Drug-Eluting Stent Trials

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SUMMARY

Background: The routine use of vascular imaging including intravascular ultrasound (IVUS) and optical coherence tomography (OCT) in guiding percutaneous coronary interventions (PCI) is still controversial especially when using drug-eluting stents. A meta-analysis of trials using bare metal stents was previously published. **Methods:** We conducted a meta-analysis of available published trials that compared imaging-guided PCI and angiography-guided PCI in patients undergoing routine PCI only. Trials that enrolled patients with acute coronary syndrome were excluded to decrease heterogeneity. We aimed to study both drug-eluting stents (DES) as well as bare metal stents (BMS). We identified seven randomized controlled trials on IVUS-guided bare metal stents. We also identified three randomized controlled trials on IVUS-guided drug-eluting stents. To improve the power of the drug-eluting stent data, we identified, and included, nine registries that compared IVUS-guided PCI to angiography-guided PCI in the drug-eluting stent era. Nonrandomized registries that included BMS only were excluded as there are multiple previous meta-analyses that studied these patients. Finally, we identified one registry that compared OCT-guided PCI to angiography-guided PCI using either a BMS or a DES. A total of 14,197 patients were studied overall. The meta-analysis was conducted using a random effect model. **Results:** Imaging guidance was associated with a significantly larger postintervention minimal luminal diameter (SMD: 0.289. 95% CI: 0.213–0.365. $P < 0.01$).Imaging-guided stenting was associated with a significant decrease in the major adverse cardiac events (MACE) in the DES patients (odds ratio: 0.810. 95% CI: 0.719–0.912. $P < 0.01$) and combined DES and BMS patients (odds ratio: 0.782. 95% CI: 0.686–0.890. $P < 0.01$). Imaging guidance was associated with significantly lower events of death from all causes in DES patients (odds ratio: 0.654. 95% CI: 0.468–0.916. $P < 0.01$) and in the combined DES and BMS patients (odds ratio: 0.727. 95% CI: 0.540–0.980. $P < 0.01$).The risk of myocardial infarction (MI) was significantly lower with imaging guidance in both, DES patients (odds ratio: 0.551. 95% CI: 0.363–0.837. $P < 0.01$) and combined DES and BMS patients (odds ratio: 0.589. 95% CI: 0.425–0.816. $P < 0.01$). This may, in part, be explained by the significantly lower risk of stent thrombosis in imaging-guided DES patients (odds ratio: 0.651. 95% CI: 0.499–0.850. $P < 0.01$) and combined DES and BMS patients (odds ratio: 0.665. 95% CI: 0.513–0.862. $P < 0.01$). Patients who received a DES showed no difference between imaging guidance and angiography guidance in repeated target lesion revascularization, while the analysis of BMS alone and the DES and BMS combined showed significant superiority of the imaging-guided PCI group. **Conclusion:** Imaging-guided PCI significantly lowered the risk of death, MI, stent thrombosis, and the combined MACE in DES-implanted patients and all stented patients (DES or BMS). However, imaging guidance had no significant effect on repeated target vessel or target lesion revascularization in patients who received DES, likely due to the effect of the drug in the stent.

Introduction

Coronary angiography is routinely employed to guide decision making in patients undergoing PCI. However, its luminological limitations are well known. Intravascular ultrasound (IVUS) is a well-established intravascular imaging tool that not only assesses the severity of luminal stenosis but also can provide an accurate description of plaque morphology and composition. More recently, optimal cohesion tomography (OCT) has been gaining traction as an invasive imaging modality in the cardiac catheterization laboratory, providing extremely high spatial resolution, and similar to IVUS, it can be of great value in optimizing PCI outcomes. The importance of using these imaging techniques is particularly paramount during complex PCI procedures and in evaluating high-risk coronary lesion subsets involving left main, ostial, or bifurcation sites.

As the introduction of IVUS, many registries and randomized controlled trials were published in attempt to evaluate the potential role of IVUS-guided percutaneous coronary intervention (PCI) on the short- and long-term clinical outcomes. The results of these trials were often contradictory, and as such this topic remains controversial (Table 1). A meta-analysis of the randomized controlled trials (RCTs) comparing IVUS-guided PCI to angiography-guided PCI in the bare metal stents (BMS) era were previously published as well as a meta-analysis of mainly registries in the drug-eluting stent (DES) era. The role of OCT-guided PCI was studied in one registry [20].

We conducted a meta-analysis of available published trials that compared imaging (IVUS and OCT)-guided PCI and angiography-guided PCI.

Method

We conducted a search of Medline and the Cochrane Library for all published, English language peer-reviewed trials published through 2014 comparing IVUS- or OCT-guided PCI to angiography-guided PCI. Two investigators did the search independently to minimize the chance of missing any studies. We aimed to include both drug-eluting stents (DES) as well as bare metal stents (BMS) trials that enrolled patients undergoing routine PCI only. Trials that enrolled patients with acute coronary syndrome, such as ADAPT-DES, were excluded to decrease heterogeneity. Small trials with low power as well as trials with poorly defined outcomes were excluded. We identified seven randomized controlled trials on IVUS-guided bare metal stents (Table 1). We also identified three randomized controlled trials on IVUS-guided drug-eluting stents (Table 1). To improve the power of the drug-eluting stent data, we identified, and included, nine well-conducted registries that compared IVUS-guided PCI to angiography–guided PCI in the drug-eluting stent era (Table 1). Nonrandomized registries that included BMS only were excluded as there are multiple previous meta-analyses that studied these patients. Finally, we identified one registry that compared OCT-guided PCI to angiography-guided PCI using either a BMS or a DES (Table 1). A total of 14,197 patients were studied overall. Least follow-up time was 6 months with an average of 20.2 months.

The meta-analysis was conducted using a random effect model to account for the heterogeneity between the different trials. The results from fixed model analysis were also reported for comparison. Odds ratio (OR) was used to compare the outcomes of binary variables. Standardized mean differences (SMD) were used for continuous variables. Forest plots for the OR and SMD were reported. The targeted endpoints included the following: death, myocardial infarction, stent thrombosis, combined major adverse cardiac events (MACE), rate of in-stent restenosis, need for target lesion revascularization and minimal luminal diameter (MLD) between the two groups. To verify that selection bias was minimal, funnel plots of the studied outcomes were performed and provided.

Results

Patients Characteristics

As previously mentioned, we pooled randomized controlled trials and registries for a total of 14,197 patients included in 20 different studies comparing an imaging-guided PCI with angiography-guided PCI. In all nonrandomized trials, we included the propensity scoring-adjusted analysis whenever available. All patients underwent elective procedures, and studies evaluating patients with acute coronary syndrome were not included.

Outcomes

Imaging guidance was associated with a significantly larger postintervention minimal luminal diameter (SMD: 0.289. 95% CI: 0.213–0.365. $P < 0.01$) (Figure S1).

Imaging-guided stenting was associated with a significant decrease in the major adverse cardiac events (MACE) in the DES patients (odds ratio: 0.810. 95% CI: 0.719–0.912. $P < 0.01$) (Figure 1A) and combined DES and BMS patients (odds ratio: 0.782. 95% CI: 0.686–0.890. $P < 0.01$) (Figure 1B). Imaging guidance was associated with significantly lower events of death from all causes in DES patients (odds ratio: 0.654. 95% CI: 0.468–0.916. $P < 0.01$) (Figure 2A) and in the combined DES and BMS patients (odds ratio: 0.727. 95% CI: 0.540–0.980. $P < 0.01$) (Figure 2B).

The risk of myocardial infarction (MI) was significantly lower with imaging guidance in both DES patients (odds ratio: 0.551. 95% CI: 0.363–0.837. $P < 0.01$) (Figure 3A) and combined DES and BMS patients (odds ratio: 0.589. 95% CI: 0.425–0.816. $P < 0.01$) (Figure 3B). This may, in part, be explained by the significantly lower risk of stent thrombosis (ST) in imaging-guided DES patients (odds ratio: 0.651. 95% CI: 0.499–0.850. $P < 0.01$) (Figure 4A) and combined DES and BMS patients (odds ratio: 0.665. 95% CI: 0.513–0.862. $P < 0.01$) (Figure 4B). Patients who received DES showed no difference between imaging guidance and angiography guidance in repeated target lesion revascularization (Figure 5A), while the analysis of BMS alone and the DES and BMS combined (Figure 5B) showed significant superiority of the imaging-guided PCI group. Funnel plots of the above studied outcomes were performed and reported (Figure S2).

Discussion

This meta-analysis combines published studies of both IVUS and OCT in both BMS and DES PCI studies in comparison with

Table 1 It summarizes all included trials and outcomes

Study number	Study name	First author	IVUS or OCT	Type	DES or BMS	Number of patients in angiography group	Number of patients in IVUS/OCT group	Time at follow-up (month)	MACE in angiography group	MACE in IVUS/OCT group	Death in angiography group	Death in IVUS/OCT group	MI in angiography group	MI in IVUS/OCT group	TLR in angiography group	TLR in IVUS/OCT group	IS thrombosis in angiography group	IS thrombosis in IVUS/OCT group	MLD in angiography group	MLD in IVUS/OCT group
1	DIPOL	Gil, R [1]	IVUS	RCT	BMS	80	83	6	13	6	1	1	4	1	6	3	NA	NA	3.06 ± 0.52	3.34 ± 0.55
2	AVID	Russo, R [2]	IVUS	RCT	BMS	369	375	12	70	68	7	12	19	25	45	30	4	5	2.9 ± 0.52	3.02 ± 0.54
3	RESIST	Schiele, F [3]	IVUS	RCT	BMS	76	79	12	28	20	1	1	NA	NA	NA	NA	NA	NA	2.46 ± 0.46	2.48 ± 0.43
4		Gaster, A [4]	IVUS	RCT	BMS	54	54	30	22	11	2	0	0	1	NA	NA	NA	NA	2.2 ± 0.5	2.3 ± 0.4
5	TULIP	Oemrawsingh, P [5]	IVUS	RCT	BMS	71	73	12	19	9	1	2	5	1	17	7	NA	NA	2.80 ± 0.31	3.01 ± 0.40
6	SIPS	Frey, A [6]	IVUS	RCT	BMS	148	121	24	55	37	4	4	6	1	43	21	NA	NA	2.38 ± 0.67	2.49 ± 0.66
7	OPTICUS	Mudra, H [7]	IVUS	RCT	BMS	275	273	12	42	49	1	5	10	6	NA	NA	NA	NA	2.91 ± 0.41	3.02 ± 0.49
8		Jakabcin, J [8]	IVUS	RCT	DES	105	105	18	12	11	2	3	4	1	6	6	6	4	NA	NA
9		Kim, J [9]	IVUS	RCT	DES	274	269	12	20	12	2	3	2	0	NA	NA	1	1	NA	NA
10	AVIO	chieffo, A [10]	IVUS	RCT	DES	142	142	24	33	24	2	0	12	10	17	13	0	1	2.51 ± 0.46	2.7 ± 0.46
11		Hru, SH [11]	IVUS	Registry	DES	1816	2765	36	270	337	98	74	18	14	NA	NA	38	50	NA	NA
12		Agostoni, P [12]	IVUS	Registry	DES	34	24	14	7	2	NA	NA	NA	NA	NA	NA	NA	NA	2.83 ± 0.5	2.93 ± 0.45
13		Chen, SL [13]	IVUS	Registry	DES	123	123	12	22	20	5	0	12	4	11	13	10	1	NA	NA
14		Claessen, B [14]	IVUS	Registry	DES	548	548	24	91	70	17	16	31	11	NA	NA	5	3	NA	NA
15		Kim, JS [15]	IVUS	Registry	DES	487	487	36	59	53	17	15	15	3	33	36	3	1	2.4 ± 0.5	2.5 ± 0.6
16		Park, KW[16]	IVUS	Registry	DES	463	463	12	14	25	3	5	3	10	8	9	1	1	2.52 ± 0.49	2.70 ± 0.44
17		Park, SJ [17]	IVUS	Registry	DES	145	145	36	40	26	14	6	13	10	NA	NA	NA	NA	NA	NA
18		Roy, P [18]	IVUS	Registry	DES	884	884	12	143	128	62	50	26	18	61	43	69	41	NA	NA
19		Kim, SH[19]	IVUS	Registry	DES	112	308	48	NA	NA	7	4	NA	NA	8	21	4	3	2.8 ± 0.5	3.0 ± 0.5
20		Prati, F [20]	OCT	Registry	DES + BMS	335	335	12	50	32	23	11	29	18	11	11	2	1	NA	NA

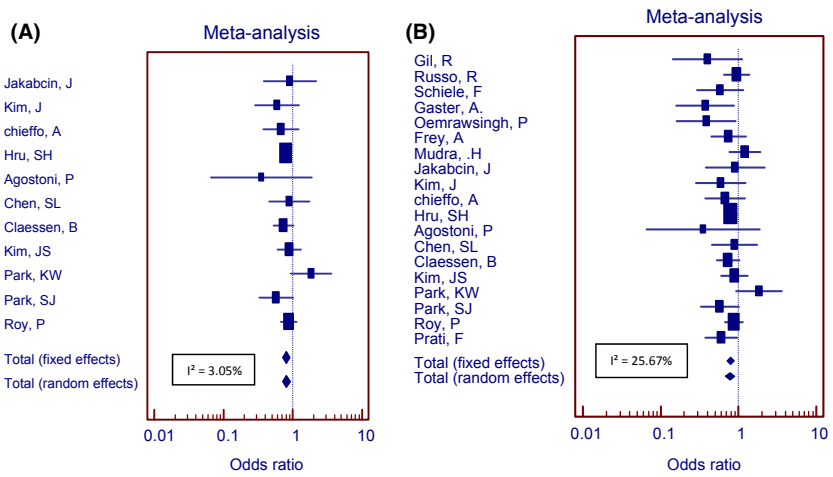

Figure 1 Analysis of MACE difference between IVUS- vs. angiography-guided PCI. (**A**) DES trials only. (**B**) DES and BMS trials.

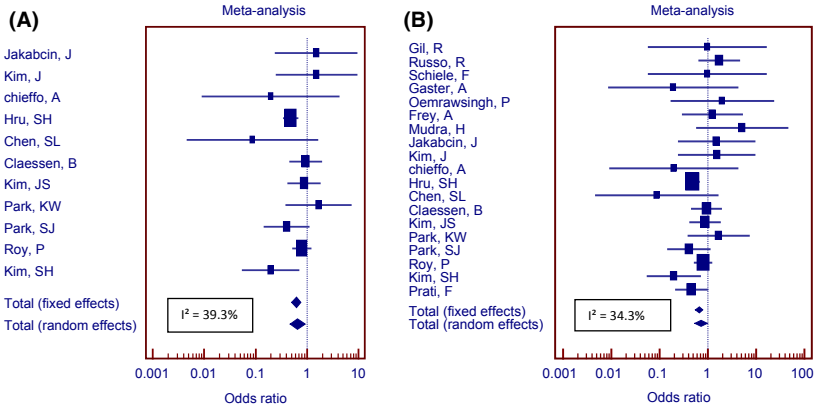

Figure 2 Analysis of death difference between IVUS- vs. angiography-guided PCI. (**A**) DES trials only. (**B**) DES and BMS trials.

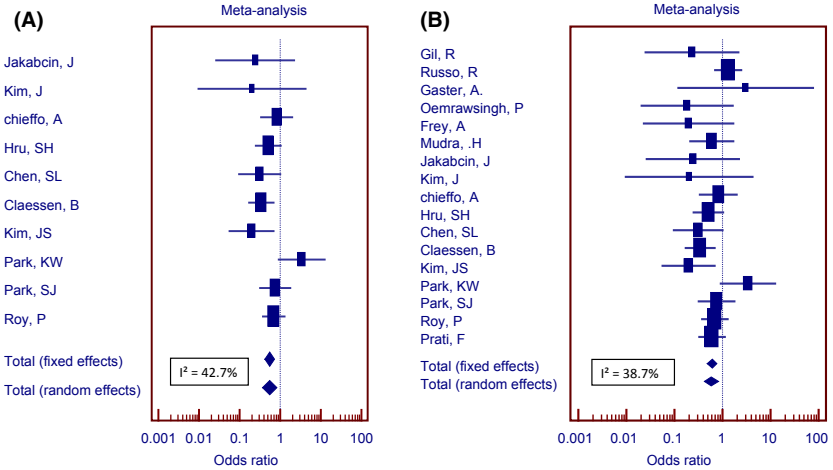

Figure 3 Analysis of MI difference between IVUS- vs. angiography-guided PCI. (**A**) DES trials only. (**B**) DES and BMS trials.

angiography guidance alone. The results demonstrated that intravascular imaging-guided PCI was associated with a significant reduction in the risk of death, MI, and ST as well as a reduced risk of the composite of death, MI, and TLR over a follow-up period averaging 20.2 months. There were lower rates of TLR with intravascular imaging compared to angiography-guided PCI only

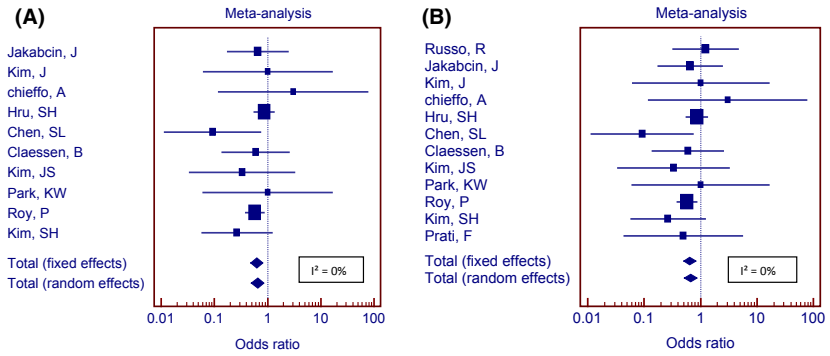

Figure 4 Analysis of in-stent thrombosis difference between IVUS- vs. angiography-guided PCI. (**A**) DES trials only. (**B**) DES and BMS trials.

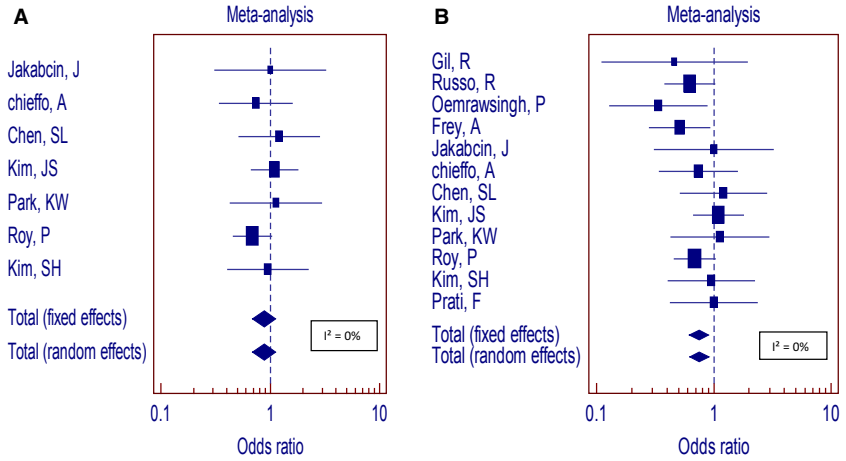

Figure 5 Analysis of TLR difference between IVUS- vs. angiography-guided PCI. (**A**) DES trials only. (**B**) DES and BMS trials.

in the pooled analysis of BMS studies as well as the combined DES and BMS studies, but not in the pooled analysis of only DES studies.

In the pre-DES era, a meta-analysis by Casella et al., in 2003, showed a significant reduction in 6 months MACE (18.7% vs., 15%, *P*: 0.03) in favor of IVUS guidance. This was predominantly driven by reduced incidence of TVR [21]. Similarly, a subsequent analysis limited to the seven randomized trials revealed that IVUS-guided PCI was associated with significant reduction in the rates of restenosis, TVR, and MACE, with no difference in MI or death [22].

In the DES era, six additional meta-analyses appeared in the literature. The analyses by Sbruzzi et al. [23] and Figueiredo Neto et al. [24] pooled eight RCTs among which only one small study included DES. Both meta-analyses reported similar results showing a significant reduction in angiographic restenosis and TLR but not in MACE with the use of IVUS versus angiography alone.

In contrast, four meta-analyses pooled only DES studies, and led to a different conclusion. Zhang et al. [25] published a DES only meta-analysis including 10 observational studies and one RCT and showed that IVUS-guided DES implantation was associated with a significant reduction in death, MACE, and ST compared with conventional angiographic guidance. Similarly, Klersy et al. [26] performed a meta-analysis including three RCT and nine observational studies in which IVUS guidance in DES implantation led to reduction in MACE, mortality, and thrombosis, but not revascularization.

A larger meta-analysis was performed by Jae-Sik Jang and collaborators who looked at three randomized trials and 12 observational studies published between 2005 and 2013 totaling 24,849 patients. The study authors concluded that the benefit of IVUS-guided over angiography-guided DES implantation was due to lower incidence of MI or death rather than a decreased rate of restenosis or revascularization [27].

Ahn et al. published the most up-to-date meta-analysis which incorporated findings from newer studies such as ADAPT-DES for evaluation of the clinical impact of IVUS-guided PCI compared with angiography-guided PCI with DES. IVUS-guided PCI was found to be associated with reduced ST, MI, TLR, and death [28]. The ADAPT-DES enrolled 8583 patients (3349 underwent IVUS-guided PCI and 5234 angiography-guided PCI). IVUS guidance led to use of more stents, larger stents or balloons, and higher inflation pressures in about 75% of patients resulting in lower rates of ST, MI, and TLR [29].

Recently, some prospective studies emerged to investigate the impact of OCT guidance in comparison with conventional angiography. However, no clinical outcomes were reported and the prospective data were limited to the extent of strut coverage. One study reported improved strut coverage and reduced mal-apposition at 6 months of follow-up with OCT-guided DES implantation [30]. Only one clinical outcome but retrospective OCT guidance study was published to date. In the multicenter CLI-OPCI trial,

OCT detected adverse findings that required further intervention in 35% of cases. OCT use was associated with significant clinical benefits; specifically, there was a significant reduction in cardiac death or MI at 1 year [20]. Considering the unique capability of OCT as an intravascular imaging modality and the potential advantages it may offer over IVUS in a variety of PCI cases, we included this study in our meta-analysis.

Consistent with the above reports, our global systematic review pooling together both IVUS and OCT intravascular imaging studies for guidance of PCI was associated with a significantly larger postintervention minimal luminal diameter, a significant decrease in the MACE in the DES patients as well as the combined DES and BMS patients. Imaging guidance was associated with significantly lower risk of death from all causes in the DES patients and the combined DES and BMS patients. The rates of MI were also significantly reduced with imaging guidance in both the DES patients and the combined DES and BMS patients.

The evidence from our meta-analyses suggests that the benefit of intravascular imaging in BMS implantation is one that has the potential to lower the incidence of repeat revascularization, but naturally such a role would be expected to recede with the use of DES due to its lower risk of restenosis. However, DES use is known to be associated with delayed intimal healing and greater propensity for stent thrombosis, especially in cases of suboptimal stent deployment such as underexpansion, mal-apposition, side branch occlusion, edge dissection, and residual plaque. Those factors are known to be mechanistic precursors of thrombotic events. Imaging guidance can identify such adverse features which can then be managed with more stents, larger stents, higher inflation pressures, or more intensive pharmacotherapy. Thus optimization of DES implantation using imaging guidance can attenuate the risks of thrombotic complications including MI and death.

Conclusion

Imaging-guided PCI significantly lowered the risk of death, MI, in-stent thrombosis, and the combined MACE in DES-implanted patients and all stented patients (DES or BMS). However, imaging guidance had no significant effect on repeated target vessel or target lesion revascularization in patients who received a DES likely due to the effect of the drug in the stent. The findings of this meta-analysis need to be confirmed in larger randomized controlled trials.

Limitations

Our meta-analysis has several limitations. Although we conducted a comprehensive search of the literature, only a limited number of randomized controlled studies were identified and included in this meta-analysis. The measured outcomes differed among some of the pooled studies, and some heterogeneity was present in the lesion and procedural characteristics. Patient-level data were not obtained, and we had to rely on the published reports in obtaining the patients' baseline and outcome data.

Conflict of Interest

The authors declare no conflict of interest.

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Supporting Information

Additional Supporting Information may be found in the online version of this article:

Figure S1. Analysis of MLD difference between IVUS- vs. angiography-guided PCI

Figure S2. Funnel plots for the different studied outcomes: (a) Funnel plot for MACE. (b) Funnel plot for death. (c) Funnel plot for in-stent thrombosis. (d) Funnel plot for myocardial infarction. (e) Funnel plot for TLR.

