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Yuan Bai

[†]These authors have contributed equally to this work and share first authorship

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An updated meta-analysis of device related thrombus following left atrial appendage closure in patients with atrial fibrillation

Song Zhang[†], Si-huai Xiong[†], Yu-gen Guan, Xian-xian Zhao, Yong-wen Qin, Zhi-fu Guo and Yuan Bai*

Department of Cardiovasology, Shanghai Changhai Hospital, Naval Medical University, Shanghai, China

Aims: Device related thrombus (DRT) is a known complication of left atrial appendage closure (LAAC). However, the relation between DRT and elevated risk of ischemic events remains controversial. This study is sought to reassessed the incidence of DRT following LAAC and the relation between DRT and elevated risk of ischemic stroke and systemic embolism (SE) with latest clinical trials included.

Methods: The PubMed, Embase, and Cochrane Library databases were systematically searched from their inception until April 2022 for studies that reported the incidence of DRT and compared the incidence of both stroke and SE between DRT patients and non-DRT patients.

Results: In 59 eligible studies, the incidence of DRT was 366/12,845 (2.8%, ranging from 0 to 11%, $l^2 = 64\%$). The incidence of DRT was not statistically different between single-seal device (SS) and dual-seal device (DS) in subgroup analysis [171/6,190 (2.8%) vs. 78/3,023 (3.6%); p = 0.93]. The pooled incidence of stroke (26 studies, 7,827 patients) in patients with and without DRT was 11.5% in DRT patients and 2.9% among non-DRT patients (OR: 5.08; 95% CI = 3.47-7.44). In the sensitivity analysis, DRT was associated with higher rate of stroke (12.1 vs. 3.2%; OR: 4.14; 95% CI = 2.69-6.38) and SE (16.0 vs. 3.8%; OR: 4.48; 95% CI = 3.04-6.62).

Conclusion: The incidence of DRT was low and similar between SS and DS devices. DRT was associated with increased rates of ischemic events. The occurrence rate of ischemic events associated DRT was comparable between two occlusion mechanism devices.

Systematic review registration: [https://www.crd.york.ac.uk/], identifier [CRD42022326179].

KEYWORDS

atrial fibrillation, left atrial appendage closure, stroke, stroke prevention, thromboembolism

Introduction

Atrial fibrillation (AF) is one of the most common arrhythmias in clinical practice among the elderly (1). Moreover, AF is related to increased risk of several serious adverse events such as ischemic stroke and systemic embolism (SE) (2). Research have shown that patients with AF are four to five times more likely to develop thrombotic and embolic events than the general population (3, 4). Therefore, stroke prevention with oral anticoagulation (OAC) and direct oral anticoagulants (DOACs) is an important part of the treatment regime in patients with AF (5). However, it might be difficult to use these drugs in the clinic, for drug interactions may increase the bleeding risk in patients. Due to these limitations, left atrial appendage closure (LAAC) is recommended for patients who are intolerant to OAC (6). Growing operator experience coupled with technical improvements and device modification have reduced procedural complications and accelerated continued growth in LAAC (7). However, device related thrombus (DRT) is still a known complication of LAAC. Until now, the prevalence and possible risk factors of DRT were discussed based on the randomized trials and large registries (8-11). Saw et al. (9) concluded that independent predictors of DRT were smoking and female sex, while Plicht et al. (10) thought CHADS₂ and CHA₂DS₂-VASc scores, platelet count, and ejection fraction were risk factors of DRT formation. Nevertheless, whether DRT increases the risk of stroke and SE remains controversial. In Cochet's study (12), a non-significant trend for a lower rate of stroke and SE was observed in DRT group rather than normal patients; while in a large multicenter RCT led by Dukkipati et al. (13) concluded that a non-significant trend for higher occurrence rate of stroke and SE was observed in DRT group. It has been less clear if and to what degree the discovery of this finding increases the stroke risk (14). Recently, major published studies focused on the incidence and consequence of DRT, hence we conducted an updated metaanalysis of both latest observational cohort and randomized controlled trials (RCT) to investigate the association of DRT following LAAC with stroke and SE. Furthermore, the subgroup analysis was performed to explore whether there was a causal relationship between DRT and device types and post-implant anti-thrombotic strategy.

Materials and methods

Search strategy

We conducted a systematic search for relevant articles in PubMed, Embase, and Cochrane Library up to April 2022. The following keywords were used: "Left Atrial Appendage Closure/ Occlusion," "device thrombosis/thrombus/embolization," "device related thrombus/ thrombosis," and "device associated thrombus/thrombosis." Both mesh terms and free terms were used to search for relevant studies. In addition, we searched the references of identified studies to find other satisfactory studies. Our meta-analysis was conducted and reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Protocols (PRISRMA-P) (15). This task was completed by two reviewers (SZ and S-HX) independently. The full text of relevant papers will be reviewed if the titles and abstracts of the articles cannot provide enough information for our inclusion. When disagreements arose, a third reviewer (X-XZ or Z-FG) was consulted. The initial study protocol was pre-registered at PROSPERO (CRD42022326179).

Inclusion and exclusion criteria

The inclusion criteria were as following: (1) Patients received LAAC with left atrial occlusion device (Watchman, ACP, or Amulet); (2) With clearly outcomes of our interest reported. The outcomes were DRT, stroke, and SE. The definition of these outcomes and the classification of devices of LAAC (16) was showed in Table 1. Specifically, the single-seal (SS) device includes Watchman, Watchman FLX, Occlutect device, and the dual-seal (DS) device includes ACP, Amulet, LAmbre device; (3) The patients were followed-up for at least 6 months; (4) At least 30 patients recruited in the study; (5) Studies were published in English.

The exclusion criteria were as following: (1) Studies which were not belong to clinical trials; (2) Studies included other interventions excluded LAAC; (3) Data from non-human species; (4) Duplicate reports with identical data; (5) The imaging detection of DRT should be performed at least 3 months after LAAC.

TABLE 1 Definition of device related thrombus (DRT), ischemic events, and classification of devices.

Terms	Definition
DRT	A well-circumscribed echoreflective mass by <i>trans</i> -esophageal echocardiographic imaging on the left atrial side of the device (during 3–12 months) (48).
Stroke	Ischemic stroke, the time of occurrence is at least 6 months after LAAC.
SE	Including ischemic stroke, TIA, and peripheral embolism (48).
Single-seal device (SS)	Including Watchman, Watchman FLX, Occlutect device.
Dual-seal device (DS)	Including ACP, Amulet, LAmbre device.

DRT, device related thrombus; SE, systemic embolism.

Quality assessment

Cochrane Collaboration risk of bias (Cochrane ROB) (17) instrument was used to perform quality assessment for the RCTs. All the observational studies were assessed using the adapted methodological items for non-randomized studies (MINORS) (18). Strictly according to the scoring criteria, two reviewers (SZ and S-HX) assessed the quality of two types of studies independently. A third reviewer (X-XZ or Z-FG) was consulted when disagreements arose.

Extraction

The data were extracted from the selected studies by two researchers (SZ and S-HX) independently. When disagreements arose, a third researcher (YB or Y-WQ) was consulted. The extracted data were as follows: first author's name, basic characteristics, LAAC device, the type of anti-thrombotic therapy, the follow-up date and protocol and the rate and diagnosis time of DRT, stroke and SE. In addition, in case of multiple studies from the same pool of patients, we will include the most recent study only (19).

Statistical analysis

We combined of each article using standard meta-analytic methods to estimate overall incidence of DRT and compared the incidence of both stroke and SE in DRT patients with non-DRT patients (defined as patients received LAAC without the occurrence of DRT). Revman (Version 5.4, The Cochrane Collaboration, London, UK) and Statistical Product and Service Solutions (SPSS) were used to analyze available data. For the incidence of DRT, stroke and SE each eligible studies, pooled estimates of odds ratio with 95% confidence interval (CI) were calculated (20, 21). The mean difference (MD) and 95% CI were used to estimate the basic characteristics of patients. Chisquare and I-square tests were used for statistical heterogeneity measurement between eligible studies. A p-value < 0.05 was considered to be statistically significant. A fixed-effects model was used if significant heterogeneity ($I^2 < 50\%$) was found among those studies. Otherwise, a random-effect model was used (22). Sensitivity analysis was performed to investigate potential source of inconsistency by including multicenter registries (MCR) and randomized controlled studies (RCT) only. Funnel plot and Begg's test were used to access publication bias (Supplementary Figure 1). Furthermore, to find out the potential predictor of DRT, eligible studies with DRT predictors [effect estimate with risk ratio (RR)] were included in secondary analysis. Separate meta-analyses were conducted for predictor variables that were reported in at least three different studies (23). When two or more RR were present per predictor, the pooled RRs with 95% CI were computed using random model (24).

Results

Search results and quality assessment

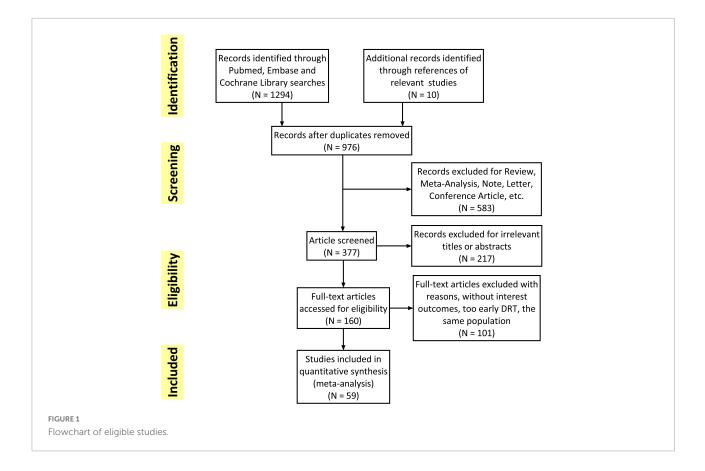
The flowchart of the study selection was presented in **Figure 1**. Overall, 1,304 studies were initially retrieved and a total of 59 studies met the inclusion criteria and were finally included. Subsequently, 101 studies were excluded because of without interest outcomes (DRT, stroke or SE), too early DRT (detection in less than 3 months) and unacceptable time for imaging follow-up. The quality of all included studies was shown in **Supplementary Table 4**. The mean MINORS score for the observational studies was 10.7 ± 1.50 . The only one RCT (25) assessed by Cochrane ROB showed low risk in all eight items.

Study characteristics

All the included studies were clinical trials with 6 months to several years follow-up. The eligible studies enrolled 12,845 patients with sample size ranging from 30 to 1,739. Most of the patients were elderly people (73.48 ± 8.64 years) and 60% of them had permanent AF. The mean CHA₂DS₂–VASc score, and HAS-BLED score was 4.11 ± 1.50 and 2.94 ± 1.19 , respectively. About the device used in appendage occlusion, 60% patients used the SS device while the remaining 40% used DS device. The total procedural success rate among all the patients was 95%. Antithrombotic therapy at discharge was OAC in 19%, DOAC in 5%, single/dual antiplatelet (SAPT/DAPT) in 48%, and other/not reported (NR) in 28%. The pooled baseline data of patients in the included studies was summarized in Table 2. The detailed data of each eligible studies was summarized in **Supplementary Table 1**.

DRT and ischemic events

A total of 12,468 (97%) patients had at least once imaging follow-up for LACC device. The number of DRT, and late DRT was 366 and 22, respectively. Among all patients included in our study, the pooled incidence of DRT was 2.8 (366/12,845), with significant variation in the reported incidence (ranging from 0 to 11.3%; $I^2 = 64\%$) (Figure 2). In the follow-up period, 314 ischemic stroke events and 439 SE were detected. Studies which reported the specific number of ischemic events between DRT patients and non-DRT patients were included for additional analysis. In the studies that reported the incidence of stroke between DRT and non-DRT (26 studies, 7,827 patients), the pooled incidence of stroke was 11.5% in DRT patients and



2.9% among non-DRT patients (OR: 5.08; 95% CI = 3.47–7.44; p < 0.001; $I^2 = 21\%$) (Figure 3A). And in the studies that reported the incidence of SE (29 studies, 7,977 patients), the pooled incidence of SE was 15.0% and 3.4% among patients without DRT (OR: 5.40; 95% CI = 3.82–7.63; p < 0.001; $I^2 = 35\%$) (Figure 3B).

Sensitivity analysis

In a sensitivity analysis, we conducted a meta-analysis to compare the incidence of ischemic events between DRT patients and non-DRT patients in MCR and RCT only. In these studies (25 studies, 9,320 patients), the pooled incidence of DRT was 2.8% (259 of 9,320) (**Supplementary Figure 2**). In the comparison of ischemic events in these studies, the DRT was associated with higher rate of stroke (12.1 vs. 3.2%; OR: 4.14; 95% CI = 2.69–6.38; p < 0.001; $I^2 = 24\%$) and SE (16.0 vs. 3.8%; OR: 4.48; 95% CI = 3.04–6.62; p < 0.001; $I^2 = 44\%$) (**Supplementary Figures 3**, 4).

Subgroup analysis

The incidence of DRT was not statistically different in patients who underwent LAAC using SS vs. DS device

[171/6,190 (2.8%) vs. 78/3,023 (3.6%); p = 0.93] (Supplementary Tables 2, 3 and Figure 4). In the subgroup analysis, the incidence of stroke (p = 0.99) and SE (p = 0.98) associated DRT was not statistically different between SS and DS devices (Figure 5). And in the subgroup analysis based on antithrombotic therapy, the difference of the incidence of DRT was similar in patients who received OAC vs. APT (p = 0.21) (Supplementary Figure 5).

Resolution of DRT

Among all the patients diagnosed with DRT, 144 patients (39%) were reported using specific regimen to treat DRT. In these patients, 16 patients (4%) received low-molecular-weight heparin (LMWH), 81 patients (22%) received OAC, and 47 patients (13%) were treated as SAPT or DAPT. In the follow-up period, most of the DRT was resolved by drugs, while only few patients (<5%) needed surgical intervention.

Predictive and non-predictive factors of DRT

Among those eligible studies, five studies (9, 13, 26-28) investigating potential predictors of DRT were included.

Age	73.48 ± 8.64
Type of atrial fibrillation	
Paroxysmal	40
Permanent	60
Hypertension	83
Diabetes mellitus	29
Previous stroke/transient ischemic attack	34
Peripheral vascular disease	22
Carotid disease	10
Coronary disease	40
Congestive heart failure	22
Chronic renal insufficiency	13
Mean CHA ₂ DS ₂ -VASc score	4.11 ± 1.50
Mean HAS-BLED score	2.94 ± 1.19
Appendage occlusion device used	
Single-seal device (SS)	60
Dual-seal device (DS)	40
Procedural success	95
Antithrombotic therapy at discharg	ge
OAC	19
DOAC	5
N/S (OAC/DOAC)	8
DA	39
SA	9
N/R	20
Number of the patients with follow-up imaging	12,468 (97)
The number of DRT	366/12,845 (2.8)
The number of late DRT (>365 days)	22
Ischemic events in the follow-up	
Stroke	314
Systemic embolism	439
DRT treatment	
LMWH	4
OAC	22
SAPT	5
DAPT	8
N/R	61

Values are mean \pm SD, %, *n* (%), or *n/N* (%). OAC, oral anticoagulation; DOAC, direct oral anticoagulants; DAPT, dual antiplatelet; LMWH, low-molecular-weight heparin; DRT, device related thrombus.

Five predictors were used in the meta-analysis, including age, smoking, history of stroke/TIA, hypertension and CHA₂DS₂– VASc score (**Figure 6**). Of the five predictors included in the

current meta-analysis, history of stroke/TIA and CHA₂DS₂– VASc score remained statistically significant (**Figures 6B**, **E**), while the other three predictors (age, smoking, and hypertension) were non-predictive after effect size aggregation (**Figures 6A**, **C**, **D**). Only the meta-analysis of smoking predictor showed high heterogeneity.

Discussion

We performed a systematic review to assess the incidence of DRT and whether detected DRT is associated with a significantly elevated risk of ischemic events. The clinical trials in our meta-analysis included more than 12,800 patients (largest-todate) and have established a solid evidence base supports that DRT is associated with a fivefold increase in ischemic events. The incidence of DRT after LAAC in included studies was 2.8%, which is lower than previous meta-analysis describing the occurrence rate of DRT (9). In the subgroup analysis of anti-thrombotic therapy, the incidence of DRT was similar between patients received post-implant APT or OAC. While the subgroup analyses based on occlusion mechanism showed the incidence of DRT was not statistically different in patients who underwent LAAC using DS or SS device. And the elevated risk of ischemic events associated DRT was not related to occlusion mechanisms of the device.

On the basis of the early successes of PROTECT-AF and PREVAIL trial, LAAC became rapidly adopted as stroke preventive strategy (20). Several major complications have been reported including pericardial tamponade and device embolization (29). However, DRT remains a major concern, with an estimated incidence of 4% (range 0-16% in eligible studies) (12, 30). In previous studies, plenty studies set 45 days after LAAC for DRT detection (31-35). However, DRT requires a certain development time after device implantation. Therefore, in combination with the definition of DRT in multiple literatures, the occurrence time of DRT was defined as at least 75 days after LAAC in our study. Studies which DRT reported within 3 months after LAAC were not included. Additionally, our meta-analysis included 59 eligible studies enrolled 12,845 patients with sample size ranging from 30 to 1,739. Compared with the previous meta-analysis, our study has included more literature published in the past 3 years. Also, more strictive definition of occurrence time was used in our study to calculate the pooled incidence of DRT. And this increased the credibility of our DRT incidence results. Therefore, the major procedurerelated complication incidence has improved over time and with increasing physician. Furtherly, improvements can be made to the current device to further reduce the incidence of DRT (WATCHMAN FLX vs. WATCHMAN 2.5; Amulet vs. ACP) (36).

Current published reports suggests that DRT is associated with a significantly elevated risk of ischemic events (9, 13, 26).

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Zhang X 2021 -3.622 0.453 2.2% 0.03 [0.01, 0.06]	-2.571		2.9%	0.08 [0.04, 0.14]				
Total (95% CI) 100.0% 0.03 (0.03, 0.04]	-3.622		2.2%	0.03 [0.01, 0.06]				
iotai (95% Ci) 100.0% 0.03 [0.03, 0.04] ▼					•			
Heterogeneity: Tau ² = 0.31; Chi ² = 159.98, df = 58 (P < 0.00001); P = 64%	Chi2 - 150.09				•	I		_
Heterogenety: Tab = 0.31; Chr = 159:36; dt = 56 (P < 0.00001); P = 64% 0.01 0.1 1 10 Test for overall effect: Z = 32.44 (P < 0.00001)		۶	~ 0.00	001), 1" - 0470	0.01 0.1	1	10	100
RE 2								

after left atrial appendage closure (LAAC) of all eligible studies. The odds ratio represents the incidence of DRT.

A significant positive association between the incidence of DRT and subsequent ischemic events was also observed in our meta-analysis, documented approximately fivefold greater rates of ischemic events in patients with DRT compared with those without DRT. Among patients who developed DRT and stroke, majority of them were diagnosed with DRT prior to the occurrence of stroke. Although different clinicians did not have a uniform opinion on the relationship between DRT and stroke, the persistent signal of increased ischemic events warrants attention. However, current result together indicate that DRT after LAAC represents a significant danger in patients with AF who are already at high risk for stroke or TIA. Ding et al. (37) suggested that the high-risk AF patients have a high rate of mortality and an ongoing significant risk of bleeding and thrombotic events during follow-up. While Teiger et al. (38) concluded that LAAC in high-risk patients seems reasonable to decrease the rate of stroke. The limitations of the uncertain definition of DRT occurrence time reduce the credibility of their results. It is noteworthy that the thrombus development after LAAC is not clear since DRT is mostly silent and its follow-up is highly depended on imaging tools. As a result, it is difficult for clinicians to diagnose the DRT occurrence time precisely. It is important to detect them in a timely manner during follow up through appropriate diagnostic imaging techniques such as coronary angiography and *trans*-esophageal echocardiography. Our findings suggest that DRT is associated with more severe complications (stroke and SE), so early diagnosis and treatment of DRT may lead to better prognosis of patients. However, some studies have shown that anticoagulant therapy has an effect on the endothelialization process (39-41), and the occurrence of DRT is related to the incomplete endothelialization of device, so the early use of anticoagulant to treat DRT may hinder the completion of endothelialization. Recent studies indicated a reduced risk of DRT in patients receiving post-LAAC anticoagulation (42).

Within the last decade, several LAAC devices have been developed and introduced into clinical practice. The included clinical trials in our study also covered 3–4 types of devices. In our study, the devices are divided into two categories, one is SS including Watchman, FLX, Occlutect, and the other is DS including ACP, Amulet, LAmbre (16). The subgroup analyses showed that the incidence of DRT was not statistically different between SS and DS group, and the occurrence rate of stroke and SE associated DRT was similar between two groups. Based on these results, it seemed that the safety for LAAC was comparable between devices under different occlusion mechanisms. As more clinical trials comparing the clinical outcomes between SS and DS devices are underway, it is important to consider not only the baseline characteristics of the patient but also the differences in device mechanisms when formulating post-operative therapy.

Identifying predictors or risk factors of DRT is important for DRT prevention. As mentioned in the preceding text, the independent predictors of DRT occurrence remained unknown. In our current meta-analysis, the predictors of DRT were history of stroke/TIA and CHA2DS2-VASc score, while the conclusion among studies were inconsistent. Saw et al. (9) concluded that smoking and female sex were independent predictors of DRT, while Plicht et al. (10) suggested that predictors might be CHADS₂ and CHA₂DS₂-VASc scores, platelet count, etc. In our previous real-world study, peri-device leak was considered as a risk factor of DRT (43). In recent two studies deep implantation depth was found to be a risk factor for DRT (7, 42). Though other predictors such as pericardial effusion and renal insufficiency were found, these predictors should be confirmed in larger studies (7). Until more data become available, researchers should raise more concern on the treatment of DRT, though the selection of treatment is still in debate. Simard et al. (44) concluded that 8-12 weeks Vitamin K antagonist (VKA), NOAC, and 2-4 weeks LMWH were recommended for treatment of DRT. Sedaghat et al. (45) revealed that patients underwent the three regimens mentioned above showed no statistical difference in clinical outcomes.

	DRT		non D			Odds Ratio		Odds F	
Study or Subgroup			Events			M-H, Fixed, 95% C		M-H, Fixed	. 95% Cl
Aminian 2019	1	9		1079	2.3%	6.01 [0.72, 50.10]			
Boersma 2017	0	28	15	997	6.2%	1.11 [0.06, 19.05]			
Chiu F 2021	0	3	4	109	2.0%	3.35 [0.15, 75.07]			
Cochet 2018	0	19	5	98	13.0%	0.44 [0.02, 8.21]	-	•	
Della 2021	2	12	5	543	1.3%	21.52 [3.72, 124.47]			
Dukkipati 2018	13	61	117	1678	46.6%	3.61 [1.90, 6.86]			
Enomoto 2016	0	3	1	423	0.2%	40.24 [1.39, 1168.96]			
Fan Y 2019	2	4	0	103	0.2%	207.00 [7.75, 5530.42]			
Fukunaga 2022	1	2	0	53	0.2%	107.00 [2.96, 3870.88]			
Guerios 2017	0	2	2	90	1.0%	7.08 [0.26, 189.34]			· · · · · ·
Huang H 2017	0	2	2	119	0.7%	9.40 [0.35, 250.97]			· · · · · ·
Huang W 2017	1	1	0	105		633.00 [9.14, 43860.71]			→
Jalal 2017	0	5	2	61	2.9%	2.16 [0.09, 50.97]			· · · · · · · · · · · · · · · · · · ·
Kebernik 2015	0	1	1	95	0.3%	21.00 [0.58, 756.41]		-	· · · · · ·
Kuroki 2020	4	17	11	513	3.9%	14.04 [3.94, 50.00]			
Ledwoch 2016	0	1	3	33	2.1%	2.90 [0.10, 85.86]			
		9	1	152					-
Li W 2022	2				0.6%	43.14 [3.48, 534.72]			``
Nguyen 2018	0	3	2	74 105	1.6%	4.14 [0.17, 103.71]			· · · ·
Osmancik 2020	0	6	9	195	4.4%	1.51 [0.08, 28.83]			````````````````````````````````
Pracoń 2018	1	5	0	92	0.3%	61.67 [2.19, 1735.88]			
Pracoń 2022	0	17	1	178	1.9%	3.38 [0.13, 86.16]			
Reddy 2013	1	6	2	136	1.0%	13.40 [1.03, 173.53]		Г	,
Regueiro 2018	0	2	6	77	2.9%	2.20 [0.10, 50.87]			-
Saw 2017	0	11	3	328	1.7%	4.04 [0.20, 82.94]			
Wiebe 2015	0	2	2	96	0.9%	7.56 [0.28, 202.09]			
Wolfrum 2016	0	12	1	157	1.6%	4.17 [0.16, 107.85]			· · · · ·
									•
Total (95% CI)		243		7584	100.0%	5.08 [3.47, 7.44]			•
Total events	28		217				T		
Heterogeneity: Chi ² =	31.84, df =	: 25 (P :	= 0.16); l ²	= 21%			0.01	0.1 1	10 100
Test for overall effect:	Z = 8.35 (F	P < 0.00	0001)				0.01		non DRT
	DRT	-	non D	RT		Odds Ratio		Odds F	atio
Study or Subgroup	Events		Events		Weight	M-H, Fixed, 95% C	1	M-H, Fixed	
Aminian 2019	2	9		1079	2.5%	9.35 [1.87, 46.78]			
Boersma 2017	0	28	20	886	7.7%	0.74 [0.04, 12.57]			
Chiu F 2021	0	20	4	109	1.7%	3.35 [0.15, 75.07]			
				98					
Cochet 2018	0	19	8		16.8%	0.27 [0.02, 4.93]			
Della 2021	3	12	9	543	1.8%	19.78 [4.58, 85.45]			
Dukkipati 2018	16	61	126	1678	39.3%	4.38 [2.41, 7.97]			
Enomoto 2016	0	3	2	423	0.2%	24.09 [0.97, 598.88]			
			0	103	0.1%	207.00 [7.75, 5530.42]			
	2	4				107.00 [2.96, 3870.88]			
Fukunaga 2022	1	2	0	53	0.2%				
Fukunaga 2022 Guerios 2017	1 0	2 2	0 2	86	0.8%	6.76 [0.25, 180.84]			
Fukunaga 2022 Guerios 2017	1	2	0						
Fukunaga 2022 Guerios 2017 Huang H 2017	1 0	2 2	0 2	86	0.8% 0.6%	6.76 [0.25, 180.84]			
Fukunaga 2022 Guerios 2017 Huang H 2017 Huang W 2017	1 0 0	2 2 2	0 2 2	86 119	0.8% 0.6%	6.76 [0.25, 180.84] 9.40 [0.35, 250.97]			
Fukunaga 2022 Guerios 2017 Huang H 2017 Huang W 2017 Jalal 2017	1 0 0 1	2 2 2 1	0 2 2 0	86 119 94	0.8% 0.6% 0.0%	6.76 [0.25, 180.84] 9.40 [0.35, 250.97] 567.00 [8.18, 39307.21]			
Fukunaga 2022 Guerios 2017 Huang H 2017 Huang W 2017 Jalal 2017 Kebernik 2015	1 0 1 0	2 2 1 5	0 2 2 0 3	86 119 94 61	0.8% 0.6% 0.0% 3.4%	6.76 [0.25, 180.84] 9.40 [0.35, 250.97] 567.00 [8.18, 39307.21] 1.52 [0.07, 33.37]			
Fukunaga 2022 Guerios 2017 Huang H 2017 Huang W 2017 Jalal 2017 Kebernik 2015 Kuroki 2020	1 0 1 0	2 2 1 5 1	0 2 0 3 1	86 119 94 61 88	0.8% 0.6% 0.0% 3.4% 0.1%	6.76 [0.25, 180.84] 9.40 [0.35, 250.97] 567.00 [8.18, 39307.21] 1.52 [0.07, 33.37] 175.00 [4.86, 6306.29]			
Fukunaga 2022 Guerios 2017 Huang H 2017 Huang W 2017 Jalal 2017 Kebernik 2015 Kuroki 2020 Ledwoch 2016	1 0 1 0 1 6	2 2 1 5 1 17	0 2 0 3 1	86 119 94 61 88 513	0.8% 0.6% 0.0% 3.4% 0.1% 2.8%	6.76 [0.25, 180.84] 9.40 [0.35, 250.97] 567.00 [8.18, 39307.21] 1.52 [0.07, 33.37] 175.00 [4.86, 6306.29] 24.89 [7.80, 79.43]			
Fukunaga 2022 Guerios 2017 Huang H 2017 Huang W 2017 Jalal 2017 Kebernik 2015 Kuroki 2020 Ledwoch 2016 Li W 2022	1 0 1 0 1 6 0 2	2 2 1 5 1 17 1 9	0 2 0 3 1 11 3 1	86 119 94 61 88 513 33 151	0.8% 0.6% 0.0% 3.4% 0.1% 2.8% 1.8% 0.5%	6.76 [0.25, 180.84] 9.40 [0.35, 250.97] 567.00 [8.18, 39307.21] 1.52 [0.07, 33.37] 175.00 [4.86, 6306.29] 24.89 [7.80, 79.43] 2.90 [0.10, 85.86] 42.86 [3.46, 531.19]			
Fukunaga 2022 Guerios 2017 Huang H 2017 Huang W 2017 Jalal 2017 Kebernik 2015 Kuroki 2020 Ledwoch 2016 Li W 2022 Matsuo 2014	1 0 1 0 1 6 0 2 0	2 2 1 5 1 17 1 9 2	0 2 0 3 1 11 3 1 1	86 119 94 61 88 513 33 151 163	0.8% 0.6% 0.0% 3.4% 0.1% 2.8% 1.8% 0.5% 0.3%	6.76 [0.25, 180.84] 9.40 [0.35, 250.97] 567.00 [8.18, 39307.21] 1.52 [0.07, 33.37] 175.00 [4.86, 6306.29] 24.89 [7.80, 79.43] 2.90 [0.10, 85.86] 42.86 [3.46, 531.19] 21.67 [0.70, 672.83]			
Fukunaga 2022 Guerios 2017 Huang H 2017 Huang W 2017 Jalal 2017 Kebernik 2015 Kuroki 2020 Ledwoch 2016 Li W 2022 Matsuo 2014 Nguyen 2018	1 0 1 0 1 6 0 2 0 0	2 2 1 5 1 17 1 9 2 3	0 2 0 3 1 11 3 1 1 2	86 119 94 61 88 513 33 151 163 74	0.8% 0.6% 0.0% 3.4% 0.1% 2.8% 1.8% 0.5% 0.3% 1.3%	6.76 [0.25, 180.84] 9.40 [0.35, 250.97] 567.00 [8.18, 39307.21] 1.52 [0.07, 33.37] 175.00 [4.86, 6306.29] 24.89 [7.80, 79.43] 2.90 [0.10, 85.86] 42.86 [3.46, 531.19] 21.67 [0.70, 672.83] 4.14 [0.17, 103.71]			
Fukunaga 2022 Guerios 2017 Huang H 2017 Huang W 2017 Jalal 2017 Kebernik 2015 Kuroki 2020 Ledwoch 2016 Li W 2022 Matsuo 2014 Nguyen 2018 Osmancik 2020	1 0 1 0 1 6 0 2 0 0 0 0 0	2 2 1 5 1 17 1 9 2 3 6	0 2 0 3 1 11 3 1 2 9	86 119 94 61 88 513 33 151 163 74 175	0.8% 0.6% 3.4% 0.1% 2.8% 1.8% 0.5% 0.3% 1.3% 4.1%	6.76 [0.25, 180.84] 9.40 [0.35, 250.97] 567.00 [8.18, 39307.21] 1.52 [0.07, 33.37] 175.00 [4.86, 6306.29] 24.89 [7.80, 79.43] 2.90 [0.10, 85.86] 42.86 [3.46, 531.19] 21.67 [0.70, 672.83] 4.14 [0.17, 103.71] 1.35 [0.07, 25.75]			
Fukunaga 2022 Guerios 2017 Huang H 2017 Huang W 2017 Jalal 2017 Kuroki 2020 Ledwoch 2016 Li W 2022 Matsuo 2014 Nguyen 2018 Osmancik 2020 Pracoń 2018	1 0 1 0 1 6 0 2 0 0 0 0 1	2 2 1 5 1 7 1 9 2 3 6 5	0 2 0 3 1 11 3 1 2 9 0	86 119 94 61 88 513 33 151 163 74 175 94	0.8% 0.6% 0.0% 3.4% 0.1% 2.8% 1.8% 0.5% 0.3% 1.3% 4.1% 0.3%	6.76 [0.25, 180.84] 9.40 [0.35, 250.97] 567.00 [8.18, 39307.21] 1.52 [0.07, 33.37] 175.00 [4.86, 6306.29] 24.89 [7.80, 79.43] 2.90 [0.10, 85.86] 42.86 [3.46, 531.19] 21.67 [0.70, 672.83] 4.14 [0.17, 103.71] 1.35 [0.07, 25.75] 63.00 [2.24, 1773.18]			
Fukunaga 2022 Guerios 2017 Huang H 2017 Huang W 2017 Jalal 2017 Kuroki 2015 Kuroki 2020 Ledwoch 2016 Li W 2022 Matsuo 2014 Nguyen 2018 Osmancik 2020 Pracoń 2018 Pracoń 2022	1 0 1 0 1 6 0 2 0 0 0 0 1 1	2 2 1 5 1 7 1 9 2 3 6 5 17	0 2 2 0 3 1 11 3 1 2 9 0 2	86 119 94 61 88 513 33 151 163 74 175 94 178	0.8% 0.6% 0.0% 3.4% 0.1% 2.8% 0.5% 0.3% 1.3% 4.1% 0.3% 2.0%	6.76 [0.25, 180.84] 9.40 [0.35, 250.97] 557.00 [8.18, 39307.21] 1.52 [0.07, 33.37] 175.00 [4.86, 6306.29] 24.89 [7.80, 79.43] 2.90 [0.10, 85.86] 42.86 [3.46, 531.19] 21.67 [0.70, 672.83] 4.14 [0.17, 103.71] 1.35 [0.07, 25.75] 63.00 [2.24, 1773.16] 5.50 [0.47, 64.02]			
Fukunaga 2022 Guerios 2017 Huang H 2017 Huang W 2017 Jalal 2017 Kebernik 2015 Kuroki 2020 Ledwoch 2016 Li W 2022 Matsuo 2014 Nguyen 2018 Osmancik 2020 Pracoń 2018 Pracoń 2022 Reddy 2013	1 0 1 0 1 6 0 2 0 0 0 0 0 1 1	2 2 1 5 1 17 1 9 2 3 6 5 17 6	0 2 2 0 3 1 11 3 1 2 9 9 0 2 2	86 119 94 61 88 513 33 151 163 74 175 94 178 136	0.8% 0.6% 0.0% 3.4% 0.1% 2.8% 0.5% 0.3% 1.3% 4.1% 0.3% 2.0% 0.8%	$\begin{array}{c} 6.76 & [0.25, 180.84]\\ 9.40 & [0.35, 250.97]\\ 567.00 & [8.18, 39307.21]\\ 1.52 & [0.07, 33.37]\\ 175.00 & [4.86, 6306.29]\\ 24.89 & [7.80, 79.43]\\ 2.90 & [0.10, 85.86]\\ 42.86 & [3.46, 531.19]\\ 21.67 & [0.70, 672.83]\\ 4.14 & [0.17, 071]\\ 1.35 & [0.07, 25.75]\\ 63.00 & [2.24, 1773.18]\\ 5.50 & [0.47, 64.02]\\ 13.40 & [1.03, 173.53]\\ \end{array}$			
Fukunaga 2022 Guerios 2017 Huang H 2017 Huang W 2017 Jalal 2017 Kebernik 2015 Kuroki 2020 Ledwoch 2016 Li W 2022 Matsuo 2014 Nguyen 2018 Osmancik 2020 Pracoń 2018 Pracoń 2022 Reddy 2013 Regueiro 2018	1 0 1 0 1 6 0 2 0 0 0 0 0 0 1 1 1	2 2 1 5 1 7 1 9 2 3 6 5 7 6 2	0 2 0 3 1 11 3 1 2 9 0 2 2 10	86 119 94 61 88 513 33 151 163 74 175 94 178 136 77	0.8% 0.6% 0.0% 3.4% 0.1% 2.8% 1.8% 0.5% 0.3% 1.3% 4.1% 0.3% 2.0% 0.8% 3.9%	6.76 [0.25, 180.84] 9.40 [0.35, 250.97] 567.00 [8.18, 39307.21] 1.52 [0.07, 33.37] 175.00 [4.86, 6306.29] 24.89 [7.80, 79.43] 2.90 [0.10, 85.86] 42.86 [3.46, 531.19] 21.67 [0.70, 672.83] 4.14 [0.17, 103.71] 1.35 [0.07, 25.75] 63.00 [2.24, 1773.18] 5.50 [0.47, 64.02] 13.40 [1.03, 173.53] 1.29 [0.06, 28.69]			
Fukunaga 2022 Guerios 2017 Huang H 2017 Huang W 2017 Jalal 2017 Kebernik 2015 Kuroki 2020 Ledwoch 2016 Li W 2022 Matsuo 2014 Nguyen 2018 Osmancik 2020 Pracoń 2018 Pracoń 2012 Reddy 2013 Regueiro 2018 Saw 2017	1 0 1 0 1 6 0 2 0 0 0 1 1 1 1 0 0	2 2 1 5 1 7 1 9 2 3 6 5 17 6 2 11	0 2 0 3 1 11 3 1 2 9 0 2 2 2 10 7	86 119 94 61 88 513 33 151 163 74 175 94 178 136 77 328	0.8% 0.6% 0.0% 3.4% 0.1% 2.8% 1.8% 0.5% 0.3% 1.3% 4.1% 0.3% 2.0% 0.8% 3.9% 3.1%	6.76 [0.25, 180.84] 9.40 [0.35, 250.97] 567.00 [8.18, 39307.21] 1.52 [0.07, 33.37] 175.00 [4.86, 6306.29] 24.89 [7.80, 79.43] 2.90 [0.10, 85.86] 42.86 [3.46, 531.19] 21.67 [0.70, 672.83] 4.14 [0.17, 103.71] 1.35 [0.07, 25.75] 63.00 [2.24, 1773.18] 5.50 [0.47, 64.02] 13.40 [1.03, 173.53] 1.29 [0.06, 28.69] 1.86 [0.10, 34.64]			
Fukunaga 2022 Guerios 2017 Huang H 2017 Huang W 2017 Jalal 2017 Kebernik 2015 Kuroki 2020 Ledwoch 2016 Li W 2022 Matsuo 2014 Nguyen 2018 Osmancik 2020 Pracoń 2018 Pracoń 2018 Reddy 2013 Regueiro 2018 Saw 2017 Sick 2007	1 0 1 0 1 6 0 2 0 0 0 0 0 1 1 1 1 0 0 1	2 2 2 2 1 5 1 5 1 1 7 1 1 9 2 3 3 6 6 5 5 17 6 2 11 4	0 2 0 3 1 11 3 1 2 9 0 2 2 2 10 7 1	86 119 94 61 88 513 33 151 163 74 175 94 175 94 136 77 328 56	0.8% 0.6% 0.0% 3.4% 0.1% 2.8% 1.8% 0.3% 1.3% 4.1% 0.3% 2.0% 0.8% 3.9% 3.1% 0.6%	$\begin{array}{c} 6.76 \left[0.25, 180.84\right]\\ 9.40 \left[0.35, 250.97\right]\\ 567.00 \left[8.18, 39307.21\right]\\ 1.52 \left[0.07, 33.37\right]\\ 175.00 \left[4.86, 6306.29\right]\\ 24.89 \left[7.80, 79.43\right]\\ 2.90 \left[0.10, 85.86\right]\\ 42.86 \left[3.46, 531.19\right]\\ 21.67 \left[0.70, 672.83\right]\\ 4.14 \left[0.17, 103.71\right]\\ 1.35 \left[0.07, 25.75\right]\\ 63.00 \left[2.24, 1773.18\right]\\ 5.50 \left[0.47, 64.02\right]\\ 13.40 \left[1.03, 173.53\right]\\ 1.29 \left[0.66, 28.69\right]\\ 1.86 \left[0.10, 34.64\right]\\ 18.33 \left[0.91, 370.28\right]\end{array}$			
Fukunaga 2022 Guerios 2017 Huang H 2017 Huang W 2017 Jalal 2017 Kuroki 2020 Ledwoch 2016 Li W 2022 Matsuo 2014 Nguyen 2018 Osmancik 2020 Pracoń 2018 Pracoń 2022 Reddy 2013 Regueiro 2018 Saw 2017 Sick 2007 Szymala 2017	1 0 1 6 0 2 0 0 0 0 0 1 1 1 1 1 0 0 0 0 0 0 0 0	2 2 2 1 5 1 1 7 1 9 9 2 3 3 6 5 5 17 6 2 11 4 5 5	0 2 2 0 3 1 11 1 3 1 1 2 9 0 2 2 2 0 7 7 1	86 119 94 61 88 513 33 151 163 74 175 94 178 136 77 328 56 72	0.8% 0.6% 0.0% 3.4% 0.1% 2.8% 1.8% 0.3% 1.3% 4.1% 0.3% 2.0% 0.8% 3.9% 3.1% 0.6% 1.3%	$\begin{array}{c} 6.76 & [0.25, 180.84]\\ 9.40 & [0.35, 250.97]\\ 567.00 & [8.18, 39307.21]\\ 1.52 & [0.07, 33.37]\\ 175.00 & [4.86, 6306.29]\\ 24.89 & [7.80, 79.43]\\ 2.90 & [0.10, 85.86]\\ 42.86 & [3.46, 531.19]\\ 21.67 & [0.70, 672.83]\\ 4.14 & [0.17, 103.71]\\ 1.35 & [0.07, 25.75]\\ 63.00 & [2.24, 1773.18]\\ 5.50 & [0.47, 64.02]\\ 13.40 & [1.03, 173.53]\\ 1.29 & [0.06, 28.69]\\ 1.86 & [0.10, 34.64]\\ 18.33 & [0.91, 370.26]\\ 4.33 & [0.16, 119.39]\\ \end{array}$			
Fukunaga 2022 Guerios 2017 Huang H 2017 Huang W 2017 Jalal 2017 Kuroki 2020 Ledwoch 2016 Li W 2022 Matsuo 2014 Nguyen 2018 Osmancik 2020 Pracoń 2018 Pracoń 2022 Reddy 2013 Regueiro 2018 Saw 2017 Sick 2007 Szymala 2017 Wiebe 2015	1 0 1 6 0 2 0 0 0 0 0 1 1 1 1 0 0 1 0 0 0 0 0 0	2 2 2 1 5 1 1 7 1 9 9 2 3 3 6 5 5 17 6 2 2 11 4 5 2	0 2 2 0 3 1 11 3 1 1 2 9 0 2 2 10 7 7 1 1 2	86 119 94 61 88 513 33 151 163 74 175 94 178 136 77 328 56 72 96	0.8% 0.6% 0.0% 3.4% 0.1% 2.8% 0.5% 0.3% 4.1% 0.3% 2.0% 0.8% 3.9% 3.9% 3.1% 0.6% 1.3%	$\begin{array}{c} 6.76 \left[0.25, 180.84\right]\\ 9.40 \left[0.35, 250.97\right]\\ 567.00 \left[8.18, 39307.21\right]\\ 1.52 \left[0.07, 33.37\right]\\ 175.00 \left[4.86, 6306.29\right]\\ 24.89 \left[7.80, 79.43\right]\\ 2.90 \left[0.10, 85.86\right]\\ 42.86 \left[3.46, 531.19\right]\\ 21.67 \left[0.70, 672.83\right]\\ 4.14 \left[0.17, 103.71\right]\\ 1.35 \left[0.07, 25.75\right]\\ 63.00 \left[2.24, 1773.16\right]\\ 5.50 \left[0.47, 64.02\right]\\ 13.40 \left[1.03, 173.53\right]\\ 1.29 \left[0.06, 28.69\right]\\ 1.86 \left[0.10, 34.64\right]\\ 18.33 \left[0.16, 119.39\right]\\ 7.56 \left[0.28, 202.09\right]\end{array}$			
Fukunaga 2022 Guerios 2017 Huang H 2017 Huang W 2017 Jalal 2017 Kebernik 2015 Kuroki 2020 Ledwoch 2016 Li W 2022 Matsuo 2014 Nguyen 2018 Oracoń 2020 Pracoń 2028 Reduły 2013 Regueiro 2018 Saw 2017 Sick 2007 Szymala 2017 Wiebe 2015	1 0 1 6 0 2 0 0 0 0 0 1 1 1 1 1 0 0 0 0 0 0 0 0	2 2 2 1 5 1 1 7 1 9 9 2 3 3 6 5 5 17 6 2 11 4 5 5	0 2 2 0 3 1 11 1 3 1 1 2 9 0 2 2 2 0 7 7 1	86 119 94 61 88 513 33 151 163 74 175 94 178 136 77 328 56 72	0.8% 0.6% 0.0% 3.4% 0.1% 2.8% 1.8% 0.3% 1.3% 4.1% 0.3% 2.0% 0.8% 3.9% 3.1% 0.6% 1.3%	$\begin{array}{c} 6.76 & [0.25, 180.84]\\ 9.40 & [0.35, 250.97]\\ 567.00 & [8.18, 39307.21]\\ 1.52 & [0.07, 33.37]\\ 175.00 & [4.86, 6306.29]\\ 24.89 & [7.80, 79.43]\\ 2.90 & [0.10, 85.86]\\ 42.86 & [3.46, 531.19]\\ 21.67 & [0.70, 672.83]\\ 4.14 & [0.17, 103.71]\\ 1.35 & [0.07, 25.75]\\ 63.00 & [2.24, 1773.18]\\ 5.50 & [0.47, 64.02]\\ 13.40 & [1.03, 173.53]\\ 1.29 & [0.06, 28.69]\\ 1.86 & [0.10, 34.64]\\ 18.33 & [0.91, 370.26]\\ 4.33 & [0.16, 119.39]\\ \end{array}$			
Fukunaga 2022 Guerios 2017 Huang H 2017 Huang W 2017 Jalal 2017 Kebernik 2015 Kuroki 2020 Ledwoch 2016 Li W 2022 Matsuo 2014 Nguyen 2018 Osmancik 2020 Pracoń 2018 Pracoń 2018 Pracoń 2022 Reddy 2013 Regueiro 2018 Saw 2017 Siok 2007 Szymala 2017 Wiebe 2015 Wolfrum 2016	1 0 1 6 0 2 0 0 0 0 0 1 1 1 1 0 0 1 0 0 0 0 0 0	2 2 2 1 5 1 7 1 9 2 3 6 5 5 17 6 2 11 4 5 2 12	0 2 2 0 3 1 11 3 1 1 2 9 0 2 2 10 7 7 1 1 2	86 119 94 61 88 513 33 151 163 74 175 94 178 136 77 328 56 72 96 157	0.8% 0.6% 0.0% 3.4% 0.1% 2.8% 0.3% 1.3% 0.3% 0.3% 0.3% 0.8% 3.1% 0.6% 1.3% 0.8% 1.3%	$\begin{array}{c} 6.76 \left[0.25, 180.84\right]\\ 9.40 \left[0.35, 250.97\right]\\ 567.00 \left[8.18, 39307.21\right]\\ 1.52 \left[0.07, 33.37\right]\\ 175.00 \left[4.86, 6306.29\right]\\ 24.89 \left[7.80, 79.43\right]\\ 2.90 \left[0.10, 85.86\right]\\ 42.86 \left[3.46, 531.19\right]\\ 21.67 \left[0.70, 672.83\right]\\ 4.14 \left[0.17, 103.71\right]\\ 1.35 \left[0.07, 25.75\right]\\ 63.00 \left[2.24, 1773.18\right]\\ 5.50 \left[0.47, 64.02\right]\\ 13.40 \left[1.03, 173.53\right]\\ 1.29 \left[0.06, 28.69\right]\\ 1.86 \left[0.10, 34.64\right]\\ 18.33 \left[0.91, 370.28\right]\\ 4.37 \left[0.16, 119.39\right]\\ 7.56 \left[0.28, 202.09\right]\\ 4.17 \left[0.16, 107.85\right]\end{array}$			
Kebernik 2015 Kuroki 2020 Ledwoch 2016 Li W 2022 Matsuo 2014 Nguyen 2018 Osmancik 2020 Pracoń 2018 Pracoń 2022 Reddy 2013 Regueiro 2018 Saw 2017 Sick 2007 Szymala 2017 Wiebe 2015 Wolfrum 2016 Total (95% CI)	1 0 1 6 0 2 0 0 0 1 1 1 1 0 0 0 1 0 0 0 0 0 0 0	2 2 2 1 5 1 1 7 1 9 9 2 3 3 6 5 5 17 6 2 2 11 4 5 2	0 2 2 2 2 2 0 3 3 1 11 3 1 11 3 1 11 1 2 9 9 0 2 2 2 10 7 7 1 1 1 2 1 1 2 1 1 1 2 1 1 1 1 2 1 1 1 1 2 1 1 1 1 2 1 1 1 1 1 2 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	86 119 94 61 88 513 33 151 163 74 175 94 178 136 77 328 56 72 96 157	0.8% 0.6% 0.0% 3.4% 0.1% 2.8% 0.5% 0.3% 4.1% 0.3% 2.0% 0.8% 3.9% 3.9% 3.1% 0.6% 1.3%	$\begin{array}{c} 6.76 \left[0.25, 180.84\right]\\ 9.40 \left[0.35, 250.97\right]\\ 567.00 \left[8.18, 39307.21\right]\\ 1.52 \left[0.07, 33.37\right]\\ 175.00 \left[4.86, 6306.29\right]\\ 24.89 \left[7.80, 79.43\right]\\ 2.90 \left[0.10, 85.86\right]\\ 42.86 \left[3.46, 531.19\right]\\ 21.67 \left[0.70, 672.83\right]\\ 4.14 \left[0.17, 103.71\right]\\ 1.35 \left[0.07, 25.75\right]\\ 63.00 \left[2.24, 1773.16\right]\\ 5.50 \left[0.47, 64.02\right]\\ 13.40 \left[1.03, 173.53\right]\\ 1.29 \left[0.06, 28.69\right]\\ 1.86 \left[0.10, 34.64\right]\\ 18.33 \left[0.16, 119.39\right]\\ 7.56 \left[0.28, 202.09\right]\end{array}$			
Fukunaga 2022 Guerios 2017 Huang H 2017 Jalal 2017 Kuroki 2020 Ledwoch 2016 Li W 2022 Matsuo 2014 Nguyen 2018 Ormancik 2020 Pracoń 2018 Pracoń 2022 Reddy 2013 Regueiro 2018 Siok 2007 Szymala 2017 Siok 2007 Szymala 2017 Wiebe 2015 Wolfrum 2016 Total (95% CI) Total events	1 0 1 6 0 2 0 0 0 0 0 1 1 1 1 1 0 0 0 1 38	2 2 2 1 5 1 1 7 1 9 2 3 6 5 5 17 6 2 2 11 4 5 2 2 12 254	0 2 2 2 2 2 2 3 3 3 1 111 3 3 1 1 11 3 1 1 1 2 2 2 2	86 119 94 61 88 513 33 151 163 74 175 94 178 136 77 328 56 72 96 157 7723	0.8% 0.6% 0.0% 2.8% 1.8% 0.5% 0.3% 1.3% 2.0% 0.8% 3.9% 0.8% 1.3% 0.6% 1.3% 0.6%	$\begin{array}{c} 6.76 \left[0.25, 180.84\right]\\ 9.40 \left[0.35, 250.97\right]\\ 567.00 \left[8.18, 39307.21\right]\\ 1.52 \left[0.07, 33.37\right]\\ 175.00 \left[4.86, 6306.29\right]\\ 24.89 \left[7.80, 79.43\right]\\ 2.90 \left[0.10, 85.86\right]\\ 42.86 \left[3.46, 531.19\right]\\ 21.67 \left[0.70, 672.83\right]\\ 4.14 \left[0.17, 103.71\right]\\ 1.35 \left[0.07, 25.75\right]\\ 63.00 \left[2.24, 1773.18\right]\\ 5.50 \left[0.47, 64.02\right]\\ 13.40 \left[1.03, 173.53\right]\\ 1.29 \left[0.06, 28.69\right]\\ 1.86 \left[0.10, 34.64\right]\\ 18.33 \left[0.91, 370.28\right]\\ 4.37 \left[0.16, 119.39\right]\\ 7.56 \left[0.28, 202.09\right]\\ 4.17 \left[0.16, 107.85\right]\end{array}$			
Fukunaga 2022 Guerios 2017 Huang H 2017 Huang W 2017 Jalal 2017 Kebernik 2015 Kuroki 2020 Ledwoch 2016 Li W 2022 Matsuo 2014 Nguyen 2018 Osmancik 2020 Pracoń 2018 Pracoń 2018 Pracoń 2018 Saw 2017 Sick 2007 Szymala 2017 Wiebe 2015 Wolfrum 2016 Total (95% CI)	1 0 1 6 0 2 0 0 0 0 0 1 1 1 1 1 0 0 0 1 8 8 42.76, df =	2 2 2 2 1 1 5 1 1 7 1 9 9 2 3 3 6 6 5 5 1 7 7 6 6 2 1 1 1 4 5 5 2 1 1 2 2 5 4 2 5 4 (P =	0 0 2 2 2 2 2 0 0 3 3 1 1 11 3 3 1 1 11 3 3 1 1 1 2 9 9 0 0 2 2 2 2 2 2 10 0 7 7 1 1 1 2 1 1 2 1 1 2 2 6 2 0 0 4 3 / P (A + A + A + A + A + A + A + A + A + A	86 119 94 61 88 513 33 151 163 74 175 94 178 136 77 328 56 72 96 157 7723	0.8% 0.6% 0.0% 2.8% 1.8% 0.5% 0.3% 1.3% 2.0% 0.8% 3.9% 0.8% 1.3% 0.6% 1.3% 0.6%	$\begin{array}{c} 6.76 \left[0.25, 180.84\right]\\ 9.40 \left[0.35, 250.97\right]\\ 567.00 \left[8.18, 39307.21\right]\\ 1.52 \left[0.07, 33.37\right]\\ 175.00 \left[4.86, 6306.29\right]\\ 24.89 \left[7.80, 79.43\right]\\ 2.90 \left[0.10, 85.86\right]\\ 42.86 \left[3.46, 531.19\right]\\ 21.67 \left[0.70, 672.83\right]\\ 4.14 \left[0.17, 103.71\right]\\ 1.35 \left[0.07, 25.75\right]\\ 63.00 \left[2.24, 1773.18\right]\\ 5.50 \left[0.47, 64.02\right]\\ 13.40 \left[1.03, 173.53\right]\\ 1.29 \left[0.06, 28.69\right]\\ 1.86 \left[0.10, 34.64\right]\\ 18.33 \left[0.91, 370.28\right]\\ 4.37 \left[0.16, 119.39\right]\\ 7.56 \left[0.28, 202.09\right]\\ 4.17 \left[0.16, 107.85\right]\end{array}$	L001		

Forest plots of stroke (A) and systemic embolism (SE) (B) in patients with device related thrombus (DRT) and non-DRT.

FIGURE 3

Study or Subgroup	log[Odds Ratio]	SF	Weight	Odds Ratio IV, Random, 95% Cl	Odds Ratio IV, Random, 95% Cl
Single-seal	<u>logiouus kanoj</u>		Weight	17, Nandolli, 3070 Ol	
Bellmann 2016	-2.639	0 732	1.7%	0.07 [0.02, 0.30]	
Boersma 2017	-2.039		6.1%	0.03 [0.02, 0.04]	-
Chen M 2020	-5.875		0.1%	0.00 [0.00, 0.05]	_
Della 2021	-3.812		4.8%	0.02 [0.01, 0.04]	
					-
Dukkipati 2018	-3.314		6.8%	0.04 [0.03, 0.05]	
Enomoto 2016	-4.949		2.3%	0.01 [0.00, 0.02]	
Fan Y 2019	-3.248	0.51	2.8%	0.04 [0.01, 0.11]	
Fukunaga 2022	-3.277	0.72	1.7%	0.04 [0.01, 0.15]	
Gu ZC 2020	-3.807		1.7%	0.02 [0.01, 0.09]	
Huang W 2017	-4.654		1.0%	0.01 [0.00, 0.07]	
Kita 2020	-2.565		2.2%	0.08 [0.02, 0.25]	
(ubo 2017	-4.069		1.7%	0.02 [0.00, 0.07]	
Kuroki 2020	-3.407		5.4%	0.03 [0.02, 0.05]	
Ledwoch 2016	-3.555		1.0%	0.03 [0.00, 0.21]	
_i W 2022		0.343	4.2%	0.06 [0.03, 0.12]	·
Mazzone 2018	-3.604		2.8%	0.03 [0.01, 0.07]	—
Vlo B 2021	-3.555	1.014	1.0%	0.03 [0.00, 0.21]	
Reddy 2013	-3.178	0.417	3.5%	0.04 [0.02, 0.09]	-
Saw_2017	-4.654	1.005	1.0%	0.01 [0.00, 0.07]	-
Sick 2007	-2.876	0.514	2.7%	0.06 [0.02, 0.15]	·
Fung K 2016	-4.543	1.422	0.5%	0.01 [0.00, 0.17]	
Niebe 2015	-3.912	0.714	1.7%	0.02 [0.00, 0.08]	—
Vintgens 2018	-4.748	0.58	2.3%	0.01 [0.00, 0.03]	
Zhang X 2021	-3.622	0.453	3.2%	0.03 [0.01, 0.06]	—
Subtotal (95% CI)			62.7%	0.03 [0.02, 0.04]	
Fest for overall effect:	Z = 31.82 (P < 0.00	001)			
	Z = 31.82 (P < 0.00	001)			
Dual-seal	Z = 31.82 (P < 0.00 -4.868		1.0%	0.01 [0.00, 0.06]	_
Dual-seal Abelson 2021	-4.868	1.004		0.01 [0.00, 0.06]	_
Dual-seal Abelson 2021 Aminian 2019	-4.868 -4.787	1.004 0.335	4.3%	0.01 [0.00, 0.02]	
Dual-seal Abelson 2021 Aminian 2019 Bertrand 2018	-4.868 -4.787 -3.638	1.004 0.335 1.013	4.3% 1.0%	0.01 [0.00, 0.02] + 0.03 [0.00, 0.19] +	_
Dual-seal Abelson 2021 Aminian 2019 Bertrand 2018 De Backer 2014	-4.868 -4.787	1.004 0.335 1.013 1.423	4.3% 1.0% 0.5%	0.01 [0.00, 0.02] 0.03 [0.00, 0.19] 0.01 [0.00, 0.19] 	-
Dual-seal Abelson 2021 Aminian 2019 Bertrand 2018 De Backer 2014 Häner 2021	-4.868 -4.787 -3.638 -4.431 -3.178	1.004 0.335 1.013 1.423 0.228	4.3% 1.0% 0.5% 5.6%	0.01 [0.00, 0.02] 0.03 [0.00, 0.19] 0.01 [0.00, 0.19] 0.04 [0.03, 0.07]	
Dual-seal Abelson 2021 Aminian 2019 Bertrand 2018 De Backer 2014 Häner 2021 Huang H 2017	-4.868 -4.787 -3.638 -4.431 -3.178 -4.324	1.004 0.335 1.013 1.423 0.228 0.712	4.3% 1.0% 0.5% 5.6% 1.7%	0.01 [0.00, 0.02] 0.03 [0.00, 0.19] 0.01 [0.00, 0.19] 0.04 [0.03, 0.07] 0.01 [0.00, 0.05]	
Dual-seal Abelson 2021 Aminian 2019 Bertrand 2018 De Backer 2014 Häner 2021 Huang H 2017 Kebernik 2015	-4.868 -4.787 -3.638 -4.431 -3.178 -4.324 -4.554	1.004 0.335 1.013 1.423 0.228 0.712 1.005	4.3% 1.0% 0.5% 5.6% 1.7% 1.0%	0.01 [0.00, 0.02] 0.03 [0.00, 0.19] 0.01 [0.00, 0.19] 0.04 [0.03, 0.07] 0.01 [0.00, 0.05] 0.01 [0.00, 0.08]	
Dual-seal Abelson 2021 Aminian 2019 Bertrand 2018 De Backer 2014 Häner 2021 Huang H 2017 Kebernik 2015 Li X 2021	-4.868 -4.787 -3.638 -4.431 -3.178 -4.324 -4.554 -3.128	1.004 0.335 1.013 1.423 0.228 0.712 1.005 0.308	4.3% 1.0% 0.5% 5.6% 1.7% 1.0% 4.6%	0.01 [0.00, 0.02] 0.03 [0.00, 0.19] 0.01 [0.00, 0.19] 0.04 [0.03, 0.07] 0.01 [0.00, 0.05] 0.01 [0.00, 0.08] 0.04 [0.02, 0.08]	
Dual-seal Abelson 2021 Aminian 2019 Bertrand 2018 De Backer 2014 Häner 2021 Huang H 2017 Kebernik 2015 Li X 2021 Park 2018	-4.868 -4.787 -3.638 -4.431 -3.178 -4.324 -4.554 -3.128 -4.787	1.004 0.335 1.013 1.423 0.228 0.712 1.005 0.308 1.42	4.3% 1.0% 0.5% 5.6% 1.7% 1.0% 4.6% 0.5%	0.01 [0.00, 0.02] 0.03 [0.00, 0.19] 0.01 [0.00, 0.19] 0.04 [0.03, 0.07] 0.01 [0.00, 0.05] 0.01 [0.00, 0.08] 0.04 [0.02, 0.08] 0.01 [0.00, 0.13]	
Dual-seal Abelson 2021 Aminian 2019 Bertrand 2018 De Backer 2014 Häner 2021 Huang H 2017 Kebernik 2015 Li X 2021 Park 2018 Plicht 2013	-4.868 -4.787 -3.638 -4.431 -3.178 -4.324 -4.554 -3.128 -4.787 -2.335	1.004 0.335 1.013 1.423 0.228 0.712 1.005 0.308 1.42 0.605	4.3% 1.0% 0.5% 5.6% 1.7% 1.0% 4.6% 0.5% 2.2%	0.01 [0.00, 0.02] 0.03 [0.00, 0.19] 0.01 [0.00, 0.19] 0.04 [0.03, 0.07] 0.01 [0.00, 0.05] 0.01 [0.00, 0.08] 0.04 [0.02, 0.08] 0.01 [0.00, 0.13] 0.10 [0.03, 0.32]	
Dual-seal Abelson 2021 Aminian 2019 Bertrand 2018 De Backer 2014 Haner 2021 Huang H 2017 Kebernik 2015 Li X 2021 Park 2018 Plicht 2013 Saw 2017	-4.868 -4.787 -3.638 -4.431 -3.178 -4.324 -4.554 -3.128 -4.787 -2.335 -3.395	1.004 0.335 1.013 1.423 0.228 0.712 1.005 0.308 1.42 0.605 0.307	4.3% 1.0% 0.5% 5.6% 1.7% 4.6% 0.5% 2.2% 4.7%	0.01 [0.00, 0.02] 0.03 [0.00, 0.19] 0.01 [0.00, 0.19] 0.04 [0.03, 0.07] 0.01 [0.00, 0.05] 0.01 [0.00, 0.08] 0.04 [0.02, 0.08] 0.01 [0.00, 0.13] 0.10 [0.03, 0.32] 0.03 [0.02, 0.06]	
Dual-seal Abelson 2021 Aminian 2019 Bertrand 2018 De Backer 2014 Häner 2021 Huang H 2017 Kebernik 2015 Li X 2021 Park 2018 Plicht 2013 Saw 2017 Szymala 2017	-4.868 -4.787 -3.638 -4.431 -3.178 -4.324 -4.554 -3.128 -4.787 -2.335 -3.395 -2.708	1.004 0.335 1.013 1.423 0.228 0.712 1.005 0.308 1.42 0.605 0.307 0.462	4.3% 1.0% 0.5% 5.6% 1.7% 4.6% 0.5% 2.2% 4.7% 3.1%	0.01 [0.00, 0.02] 0.03 [0.00, 0.19] 0.01 [0.00, 0.19] 0.04 [0.03, 0.07] 0.01 [0.00, 0.05] 0.01 [0.00, 0.08] 0.04 [0.02, 0.08] 0.01 [0.00, 0.13] 0.10 [0.03, 0.32] 0.03 [0.02, 0.06] 0.07 [0.03, 0.16]	
Dual-seal Abelson 2021 Aminian 2019 Bertrand 2018 De Backer 2014 Häner 2021 Huang H 2017 Kebernik 2015 Li X 2021 Park 2018 Plicht 2013 Saw 2017 Szymala 2017 Jrena 2013	-4.868 -4.787 -3.638 -4.431 -3.178 -4.324 -4.554 -3.128 -4.787 -2.335 -3.395 -2.708 -4.644	1.004 0.335 1.013 1.423 0.228 0.712 1.005 0.308 1.42 0.605 0.307 0.462 1.421	4.3% 1.0% 0.5% 5.6% 1.7% 4.6% 0.5% 4.7% 3.1% 0.5%	0.01 [0.00, 0.02] 0.03 [0.00, 0.19] 0.01 [0.00, 0.19] 0.04 [0.03, 0.07] 0.01 [0.00, 0.05] 0.01 [0.00, 0.08] 0.04 [0.02, 0.08] 0.01 [0.00, 0.13] 0.10 [0.03, 0.32] 0.03 [0.02, 0.06] 0.07 [0.03, 0.16] 0.01 [0.00, 0.16]	
Dual-seal Abelson 2021 Aminian 2019 Bertrand 2018 De Backer 2014 Haner 2021 Huang H 2017 Kebernik 2015 Li X 2021 Park 2018 Plicht 2013 Saw 2017 Szymala 2017 Jrena 2013 Wang G 2020	-4.868 -4.787 -3.638 -4.431 -3.178 -4.324 -4.554 -3.128 -4.787 -2.335 -3.395 -2.708 -4.644 -3.296	1.004 0.335 1.013 1.423 0.228 0.712 1.005 0.308 1.42 0.605 0.307 0.462 1.421 0.72	4.3% 1.0% 0.5% 5.6% 1.7% 4.6% 0.5% 4.7% 3.1% 0.5% 1.7%	0.01 [0.00, 0.02] 0.03 [0.00, 0.19] 0.01 [0.00, 0.19] 0.04 [0.03, 0.07] 0.01 [0.00, 0.05] 0.01 [0.00, 0.08] 0.04 [0.02, 0.08] 0.01 [0.00, 0.13] 0.10 [0.03, 0.32] 0.03 [0.02, 0.06] 0.07 [0.03, 0.16] 0.01 [0.00, 0.16] 0.04 [0.01, 0.15]	
Dual-seal Abelson 2021 Aminian 2019 Bertrand 2018 De Backer 2014 Haner 2021 Huang H 2017 Kebernik 2015 Li X 2021 Park 2018 Plicht 2013 Saw 2017 Szymala 2017 Jrena 2013 Wang G 2020 Wolfrum 2016	-4.868 -4.787 -3.638 -4.431 -3.178 -4.324 -4.554 -3.128 -4.787 -2.335 -3.395 -2.708 -4.644	1.004 0.335 1.013 1.423 0.228 0.712 1.005 0.308 1.42 0.605 0.307 0.462 1.421	4.3% 1.0% 0.5% 5.6% 1.7% 4.6% 0.5% 2.2% 4.7% 3.1% 0.5% 1.7% 4.7%	0.01 [0.00, 0.02] 0.03 [0.00, 0.19] 0.01 [0.00, 0.19] 0.04 [0.03, 0.07] 0.01 [0.00, 0.05] 0.01 [0.00, 0.08] 0.04 [0.02, 0.08] 0.01 [0.00, 0.13] 0.10 [0.03, 0.32] 0.03 [0.02, 0.06] 0.07 [0.03, 0.16] 0.01 [0.00, 0.16] 0.04 [0.01, 0.15] 0.08 [0.04, 0.14]	
Dual-seal Abelson 2021 Aminian 2019 Bertrand 2018 De Backer 2014 Häner 2021 Huang H 2017 Kebernik 2015 Li X 2021 Park 2018 Plicht 2013 Saw 2017 Szymala 2017 Jrena 2013 Nang G 2020 Nolfrum 2016 Subtotal (95% CI)	-4.868 -4.787 -3.638 -4.431 -3.178 -4.324 -4.554 -3.128 -4.787 -2.335 -3.395 -2.708 -4.644 -3.296 -2.571	1.004 0.335 1.013 1.423 0.228 0.712 1.005 0.308 1.42 0.605 0.307 0.462 1.421 0.72 0.3	4.3% 1.0% 0.5% 5.6% 1.7% 4.6% 0.5% 2.2% 4.7% 3.1% 0.5% 1.7% 4.7% 37.3%	0.01 [0.00, 0.02] 0.03 [0.00, 0.19] 0.01 [0.00, 0.19] 0.04 [0.03, 0.07] 0.01 [0.00, 0.05] 0.01 [0.00, 0.08] 0.04 [0.02, 0.08] 0.01 [0.00, 0.13] 0.10 [0.03, 0.32] 0.03 [0.02, 0.06] 0.07 [0.03, 0.16] 0.01 [0.00, 0.16] 0.04 [0.01, 0.15] 0.08 [0.04, 0.14] 0.03 [0.02, 0.05]	
Dual-seal Abelson 2021 Aminian 2019 Bertrand 2018 De Backer 2014 Häner 2021 Huang H 2017 Kebernik 2015 Li X 2021 Park 2018 Plicht 2013 Saw 2017 Szymala 2017 Urena 2013 Wang G 2020 Wolfrum 2016 Subtotal (95% CI) Heterogeneity: Tau ² =	-4.868 -4.787 -3.638 -4.431 -3.178 -4.324 -4.554 -3.128 -4.787 -2.335 -2.708 -4.644 -3.296 -2.571 0.39; Chi ² = 39.11,	1.004 0.335 1.013 1.423 0.228 0.712 1.005 0.308 1.42 0.605 0.307 0.462 1.421 0.72 0.3 df = 14	4.3% 1.0% 0.5% 5.6% 1.7% 4.6% 0.5% 2.2% 4.7% 3.1% 0.5% 1.7% 4.7% 37.3%	0.01 [0.00, 0.02] 0.03 [0.00, 0.19] 0.01 [0.00, 0.19] 0.04 [0.03, 0.07] 0.01 [0.00, 0.05] 0.01 [0.00, 0.08] 0.04 [0.02, 0.08] 0.01 [0.00, 0.13] 0.10 [0.03, 0.32] 0.03 [0.02, 0.06] 0.07 [0.03, 0.16] 0.01 [0.00, 0.16] 0.04 [0.01, 0.15] 0.08 [0.04, 0.14] 0.03 [0.02, 0.05]	
Test for overall effect: Dual-seal Abelson 2021 Aminian 2019 Bertrand 2018 De Backer 2014 Häner 2021 Huang H 2017 Kebernik 2015 Li X 2021 Park 2018 Plicht 2013 Saw 2017 Szymala 2017 Urena 2013 Wang G 2020 Wolfrum 2016 Subtotal (95% CI) Heterogeneity: Tau ² = Test for overall effect: Total (95% CI)	-4.868 -4.787 -3.638 -4.431 -3.178 -4.324 -4.554 -3.128 -4.787 -2.335 -3.395 -2.708 -4.644 -3.296 -2.571 0.39; Chi ² = 39.11, Z = 15.32 (P < 0.00	1.004 0.335 1.013 1.423 0.228 0.712 1.005 0.308 1.42 0.605 0.307 0.462 1.421 0.72 0.3 df = 14 001)	4.3% 1.0% 0.5% 5.6% 1.7% 4.6% 0.5% 2.2% 4.7% 3.1% 0.5% 1.7% 3.7.3% (P = 0.000	0.01 [0.00, 0.02] 0.03 [0.00, 0.19] 0.01 [0.00, 0.19] 0.04 [0.03, 0.07] 0.01 [0.00, 0.05] 0.01 [0.00, 0.08] 0.04 [0.02, 0.08] 0.01 [0.00, 0.13] 0.10 [0.03, 0.32] 0.03 [0.02, 0.06] 0.07 [0.03, 0.16] 0.01 [0.00, 0.16] 0.04 [0.01, 0.15] 0.08 [0.04, 0.14] 0.03 [0.02, 0.04] 0.03 [0.02, 0.04]	
Dual-seal Abelson 2021 Aminian 2019 Bertrand 2018 De Backer 2014 Häner 2021 Huang H 2017 Kebernik 2015 Li X 2021 Park 2018 Plicht 2013 Saw 2017 Szymala 2017 Urena 2013 Wang G 2020 Wolfrum 2016 Subtotal (95% CI) Heterogeneity: Tau ² = Test for overall effect: Total (95% CI) Heterogeneity: Tau ² =	$\begin{array}{c} -4.868\\ -4.787\\ -3.638\\ -4.431\\ -3.178\\ -4.324\\ -4.554\\ -3.128\\ -4.787\\ -2.335\\ -3.395\\ -2.708\\ -4.644\\ -3.296\\ -2.571\\ 0.39; Chi^2 = 39.11,\\ Z = 15.32 \ (P < 0.00\\ 0.15; Chi^2 = 71.27, \end{array}$	1.004 0.335 1.013 1.423 0.228 0.712 1.005 0.308 1.42 0.605 0.307 0.462 1.421 0.72 0.3 df = 14 0001)	4.3% 1.0% 0.5% 5.6% 1.7% 4.6% 0.5% 2.2% 4.7% 3.1% 0.5% 1.7% 3.7.3% (P = 0.000	0.01 [0.00, 0.02] 0.03 [0.00, 0.19] 0.01 [0.00, 0.19] 0.04 [0.03, 0.07] 0.01 [0.00, 0.05] 0.01 [0.00, 0.08] 0.04 [0.02, 0.08] 0.01 [0.00, 0.13] 0.10 [0.03, 0.32] 0.03 [0.02, 0.06] 0.07 [0.03, 0.16] 0.04 [0.01, 0.15] 0.08 [0.04, 0.14] 0.03 [0.02, 0.05] 0.03 [0.02, 0.04] 0.03 [0.02, 0.04]	
Dual-seal Abelson 2021 Aminian 2019 Bertrand 2018 De Backer 2014 Häner 2021 Huang H 2017 Kebernik 2015 Li X 2021 Park 2018 Plicht 2013 Saw 2017 Szymala 2017 Urena 2013 Wang G 2020 Wolfrum 2016 Subtotal (95% CI) Heterogeneity: Tau ² = Test for overall effect:	-4.868 -4.787 -3.638 -4.431 -3.178 -4.324 -4.554 -3.128 -4.787 -2.335 -3.395 -2.708 -4.644 -3.296 -2.571 0.39; Chi ² = 39.11, Z = 15.32 (P < 0.00 0.15; Chi ² = 71.27, Z = 32.88 (P < 0.00	1.004 0.335 1.013 1.423 0.228 0.712 1.005 0.308 1.42 0.605 0.307 0.462 1.421 0.72 0.3 df = 14 0001) df = 38 001)	4.3% 1.0% 0.5% 5.6% 1.7% 1.0% 4.6% 0.5% 2.2% 4.7% 3.1% 0.5% 1.7% 4.7% 3.1% 0.5% 1.7% 4.7% 3.1% 0.5% (P = 0.000	$\begin{array}{c} 0.01 \ [0.00, 0.02] \\ 0.03 \ [0.00, 0.19] \\ 0.01 \ [0.00, 0.19] \\ 0.04 \ [0.03, 0.07] \\ 0.01 \ [0.00, 0.05] \\ 0.01 \ [0.00, 0.08] \\ 0.04 \ [0.02, 0.08] \\ 0.04 \ [0.02, 0.08] \\ 0.01 \ [0.00, 0.13] \\ 0.01 \ [0.00, 0.13] \\ 0.01 \ [0.00, 0.13] \\ 0.03 \ [0.02, 0.06] \\ 0.07 \ [0.03, 0.16] \\ 0.01 \ [0.00, 0.16] \\ 0.04 \ [0.01, 0.15] \\ 0.08 \ [0.04, 0.14] \\ 0.03 \ [0.02, 0.05] \\ 0.01 \ [0.02, 0.04] \\ 0.01 \ [0.00, 0.16] \\ 0.01 \ [0.02, 0.04] \\ 0.01 \ [0.01, 0.15] \\ 0.03 \ [0.02, 0.04] \\ 0.01 \ [0.01, 0.15] \\ 0.03 \ [0.02, 0.04] \\ 0.01 \ [0.01, 0.15] \\ 0.01 \ [0.01, 0.15] \\ 0.01 \ [0.01, 0.15] \\ 0.01 \ [0.01, 0.15] \\ 0.01 \ [0.01, 0.15] \\ 0.01 \ [0.01, 0.15] \\ 0.01 \ [0.01, 0.15] \\ 0.01 \ [0.01, 0.15] \\ 0.01 \ [0.01, 0.15] \\ 0.01 \ [0.01, 0.15] \\ 0.01 \ [0.01, 0.15] \\ 0.01 \ [0.01, 0.15] \\ 0.01 \ [0.01, 0.15] \\ 0.01 \ [0.01, 0.15] \\ 0.01 \ [0.01, 0.15] \\ 0.01 \ [0.01, 0.15] \\ 0.01 \ [0.01, 0.15] \\ 0.01 \ [0.01, 0.15] \\ 0.01 \ [0.01, 0.15] \\ 0.01 \ [0.01, 0.15] \\ 0.01 \ [0.01, 0.15] \\ 0.01 \ [0.01, 0.15] \\ 0.01 \ [0.01, 0.15] \\ 0.01 \ [0.01, 0.15] \\ 0.01 \ [0.01, 0.15] \\ 0.01 \ [0.01, 0.15] \\ 0.01 \ [0.01, 0.15] \\ 0.01 \ [0.01, 0.15] \\ 0.01 \ [0.01, 0.15] \\ 0.01 \ [0.01, 0.15] \\ 0.01 \ [0.01, 0.15] \\ 0.01 \ [0.01, 0.15] \\ 0.01 \ [0.01, 0.15] \\ 0.01 \ [0.01, 0.15] \\ 0.01 \ [0.01, 0.15] \\ 0.01 \ [0.01, 0.15] \\ 0.01 \ [0.01, 0.15] \\ 0.01 \ [0.01, 0.15] \\ 0.01 \ [0.01, 0.15] \\ 0.01 \ [0.01, 0.15] \\ 0.01 \ [0.01, 0.15] \\ 0.01 \ [0.01, 0.15] \\ 0.01 \ [0.01, 0.15] \\ 0.01 \ [0.01, 0.15] \\ 0.01 \ [0.01, 0.15] \\ 0.01 \ [0.01, 0.15] \\ 0.01 \ [0.01, 0.15] \\ 0.01 \ [0.01, 0.15] \\ 0.01 \ [0.01, 0.15] \\ 0.01 \ [0.01, 0.15] \\ 0.01 \ [0.01, 0.15] \\ 0.01 \ [0.01, 0.15] \\ 0.01 \ [0.01, 0.15] \\ 0.01 \ [0.01, 0.15] \\ 0.01 \ [0.01, 0.15] \\ 0.01 \ [0.01, 0.15] \\ 0.01 \ [0.01, 0.15] \\ 0.01 \ [0.01, 0.15] \\ 0.01 \ [0.01, 0.15] \\ 0.01 \ [0.01, 0.15] \\ 0.01 \ [0.01, 0.15] \\ 0.01 \ [0.01, 0.15] \\ 0.01 \ [0.01, 0.15] \\ 0.01 \ [0.01, 0.15] \\ 0.01 \ [0.01, 0.15] \\ 0.01 \ [0.01, 0.15] \\ 0.01 \ [0.01, 0.15] \\ 0.01 \ [0.01, 0.15] \\ 0.01 \ [0.01, 0$	

	DRT		non D			Odds Ratio	Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI	M-H, Fixed, 95% Cl
Single-seal							
Boersma 2017	0	28	15	997	8.9%	1.11 [0.06, 19.05]	
Della 2021	2	12	5	543	1.9%	21.52 [3.72, 124.47]	
Dukkipati 2018	13	61	117	1678	66.7%	3.61 [1.90, 6.86]	-∎ -
Enomoto 2016	0	3	1	423	0.3%	40.24 [1.39, 1168.96]	
Fan Y 2019	2	4	0	103	0.2%	207.00 [7.75, 5530.42]	
Fukunaga 2022	1	2	0	53	0.3%	107.00 [2.96, 3870.88]	
Huang W 2017	1	1	0	105	0.0%	633.00 [9.14, 43860.71]	
Kuroki 2020	4	17	11	513	5.6%	14.04 [3.94, 50.00]	
Ledwoch 2016	0	1	3	33	3.0%	2.90 [0.10, 85.86]	
							→
Li W 2022	2	9	1	152	0.9%	43.14 [3.48, 534.72]	
Reddy 2013	1	6	2	136	1.5%	13.40 [1.03, 173.53]	
Wiebe 2015	0	2	2	96	1.3%	7.56 [0.28, 202.09]	
Subtotal (95% CI)		146		4832	90.4%	6.24 [4.01, 9.70]	•
Total events	26		157				
Heterogeneity: Chi2 =	23.02, df =		= 0.02); l²	= 52%			
Test for overall effect:	Z = 8.13 (F	P < 0.0	0001)				
Dual-seal							
		~	00	4070	0.001	0.04 10 70 50 100	
Aminian 2019	1	9	22	1079	3.3%	6.01 [0.72, 50.10]	
Huang H 2017	0	2	2	119	1.0%	9.40 [0.35, 250.97]	
Kebernik 2015	0	1	1	95	0.5%	21.00 [0.58, 756.41]	
Saw 2017	0	11	3	328	2.4%	4.04 [0.20, 82.94]	
Wolfrum 2016	0	12	1	157	2.3%	4.17 [0.16, 107.85]	
Subtotal (95% Cl)	0	35		1778	9.6%	6.19 [1.72, 22.32]	
		55	-	1770	0.070	0.10 [1.72, 22.02]	-
Total events	1		29				
Heterogeneity: Chi ² =				0%			
Test for overall effect:	Z = 2.78 (F	P = 0.0	05)				
Total (95% CI)		181		6610	100.0%	6.23 [4.11, 9.46]	•
Total events	27		186				
		40.0					
Heterogeneity: Chi ² =				= 32%			0.01 0.1 1 10 100
Test for overall effect:	7 = 8.59 (F						
Test for subaroup diffe	erences: Cl	ni² = 0.1	00. df = 1		99). I ² = (DRT non DRT
B Study or Subgroup	erences: Cl	ni² = 0.	,	RT		Odds Ratio M-H. Fixed, 95% Cl	Odds Ratio
B Study or Subgroup Single-seal	erences: Cl DRT Events	ni² = 0. Total	00. df = 1 non D Events	RT Total	Weight	Odds Ratio M-H. Fixed, 95% CI	Odds Ratio
B Study or Subgroup	erences: Cl	ni² = 0.	00. df = 1 non D	RT		Odds Ratio	Odds Ratio
B Study or Subgroup Single-seal	erences: Cl DRT Events	ni² = 0. Total	00. df = 1 non D Events	RT Total	Weight	Odds Ratio M-H. Fixed, 95% CI	Odds Ratio
B <u>Study or Subgroup</u> Single-seal Boersma 2017	erences: Cl DRT Events 0	ni² = 0.1 <u>Total</u> 28	00. df = 1 non D <u>Events</u> 20	RT <u>Total</u> 886	Weight 11.9%	Odds Ratio M-H. Fixed. 95% CI 0.74 [0.04, 12.57]	Odds Ratio
B Study or Subgroup Single-seal Boersma 2017 Della 2021	erences: Cl DRT Events 0 3	ni² = 0 Total 28 12	00. df = 1 non D <u>Events</u> 20 9 126	RT <u>Total</u> 886 543	<u>Weight</u> 11.9% 2.7%	Odds Ratio <u>M-H. Fixed. 95% Cl</u> 0.74 (0.04, 12.57) 19.78 (4.58, 85.45) 4.38 (2.41, 7.97)	Odds Ratio
B Single-seal Boersma 2017 Della 2021 Dukkipati 2018 Enomoto 2016	erences: Cl DRT Events 0 3 16 0	ni ² = 0. Total 28 12 61 3	00. df = 1 non D <u>Events</u> 20 9 126 2	RT Total 886 543 1678 423	Weight 11.9% 2.7% 60.7% 0.4%	Odds Ratio M-H. Fixed. 95% CI 0.74 [0.04, 12.57] 19.78 [4.58, 85.45] 4.38 [2.41, 7.97] 24.09 [0.97, 598.88]	Odds Ratio
B Single-seal Boersma 2017 Della 2021 Dukkipati 2018 Enomoto 2016 Fan Y 2019	erences: Cl DRT Events 0 3 16 0 2	ni ² = 0 Total 28 12 61 3 4	00. df = 1 non D <u>Events</u> 20 9 126 2 0	RT Total 886 543 1678 423 103	Weight 11.9% 2.7% 60.7% 0.4% 0.2%	Odds Ratio M-H. Fixed. 95% Cl 0.74 [0.04, 12.57] 19.78 [4.58, 85.45] 4.38 [2.41, 7.97] 24.09 [0.97, 598.88] 207.00 [7.75, 5530.42]	Odds Ratio
B Single-seal Boersma 2017 Della 2021 Dukkipati 2018 Enomoto 2016 Fan Y 2019 Fukunaga 2022	erences: Cl DRT <u>Events</u> 0 3 16 0 2 1	ni ² = 0 Total 28 12 61 3 4 2	00. df = 1 non D <u>Events</u> 20 9 126 2 0 0	RT Total 886 543 1678 423 103 53	Weight 11.9% 2.7% 60.7% 0.4% 0.2% 0.2%	Odds Ratio M-H. Fixed. 95% CI 19.78 [4.58, 85.45] 4.38 [2.41, 7.97] 24.09 [0.97, 598.88] 207.00 [7.75, 5530.42] 107.00 [2.96, 3870.88]	Odds Ratio
B Single-seal Boersma 2017 Della 2021 Dukkipati 2018 Enomoto 2016 Fan Y 2019 Fukunaga 2022 Huang W 2017	erences: Cl DRT <u>Events</u> 0 3 16 0 2 1 1	ni ² = 0.1 Total 28 12 61 3 4 2 1	00. df = 1 non D Events 20 9 126 2 0 0 0 0 0	RT Total 886 543 1678 423 103 53 94	Weight 11.9% 2.7% 60.7% 0.4% 0.2% 0.2% 0.0%	Odds Ratio M-H. Fixed. 95% Cl 0.74 [0.04, 12.57] 19.78 [4.58, 85.45] 4.38 [2.41, 7.97] 24.09 [0.97, 598.88] 207.00 [7.75, 5530.42] 107.00 [2.96, 3870.88] 567.00 [8.18, 39307.21]	Odds Ratio
B Single-seal Boersma 2017 Della 2021 Dukkipati 2018 Enomoto 2016 Fan Y 2019 Fukunaga 2022 Huang W 2017 Kuroki 2020	DRT Events 0 3 16 0 2 1 1 6	ni ² = 0. Total 28 12 61 3 4 2 1 17	00. df = 1 non D <u>Events</u> 20 9 126 2 0 0 0 0 11	RT Total 886 543 1678 423 103 53 94 513	Weight 11.9% 2.7% 60.7% 0.4% 0.2% 0.2% 0.0% 4.2%	Odds Ratio M-H. Fixed. 95% Cl 0.74 [0.04, 12.57] 19.78 [4.58, 85.45] 4.38 [2.41, 7.97] 24.09 [0.97, 598.88] 207.00 [7.75, 5530.42] 107.00 [2.96, 3670.88] 567.00 [8.18, 39307.21] 24.89 [7.80, 79.43]	Odds Ratio
B Study or Subgroup Single-seal Boersma 2017 Della 2021 Dukkipati 2018 Enomoto 2016 Fan Y 2019 Fukunaga 2022 Huang W 2017 Kuroki 2020 Ledwoch 2016	DRT Events 0 3 16 0 2 1 6 0	Total 28 12 61 3 4 2 1 17 17	00. df = 1 non D <u>Events</u> 20 9 126 2 0 0 0 0 11 3	RT Total 886 543 1678 423 103 53 94 513 33	Weight 11.9% 2.7% 60.7% 0.4% 0.2% 0.2% 0.0% 4.2% 2.7%	Odds Ratio M-H. Fixed. 95% CI 0.74 [0.04, 12.57] 19.78 [4.58, 85.45] 4.38 [2.41, 7.97] 24.09 [0.97, 598.88] 207.00 [7.75, 5530.42] 107.00 [2.96, 3870.88] 567.00 [8.18, 39307.21] 24.89 [7.80, 7.9.43] 2.90 [0.10, 85.86]	Odds Ratio
B Study or Subgroup Single-seal Boersma 2017 Della 2021 Dukkipati 2018 Enomoto 2016 Fan Y 2019 Fukunaga 2022 Huang W 2017 Kuroki 2020 Ledwoch 2016 Li W 2022	erences: CI DRT <u>Events</u> 0 3 16 0 2 1 1 6 0 2 2 1 1 6 0 2 2	Total 28 12 61 3 4 2 1 17 19	00. df = 1 non D Events 20 9 126 2 0 0 0 0 11 3 1	RT Total 886 543 1678 423 103 53 94 513 33 151	Weight 11.9% 2.7% 60.7% 0.4% 0.2% 0.2% 0.2% 0.0% 4.2% 2.7% 0.8%	Odds Ratio M-H. Fixed. 95% Cl 0.74 [0.04, 12.57] 19.78 [4.58 84.55] 4.38 [2.41, 7.97] 24.09 [0.97, 598.88] 207.00 [7.75, 5530.42] 107.00 [2.96, 3870.88] 567.00 [8.18, 39307.21] 24.89 [7.80, 79.43] 2.90 [0.10, 85.86] 42.86 [3.46, 531.19]	Odds Ratio
B Study or Subgroup Single-seal Boersma 2017 Della 2021 Dukkipati 2018 Enomoto 2016 Fan Y 2019 Fukunaga 2022 Huang W 2017 Kuroki 2020 Ledwoch 2016	DRT Events 0 3 16 0 2 1 6 0	Total 28 12 61 3 4 2 1 17 17	00. df = 1 non D <u>Events</u> 20 9 126 2 0 0 0 0 11 3	RT Total 886 543 1678 423 103 53 94 513 33	Weight 11.9% 2.7% 60.7% 0.4% 0.2% 0.2% 0.0% 4.2% 2.7%	Odds Ratio M-H. Fixed. 95% CI 0.74 [0.04, 12.57] 19.78 [4.58, 85.45] 4.38 [2.41, 7.97] 24.09 [0.97, 598.88] 207.00 [7.75, 5530.42] 107.00 [2.96, 3870.88] 567.00 [8.18, 39307.21] 24.89 [7.80, 7.9.43] 2.90 [0.10, 85.86]	Odds Ratio
B Study or Subgroup Single-seal Boersma 2017 Della 2021 Dukkipati 2018 Enomoto 2016 Fan Y 2019 Fukunaga 2022 Huang W 2017 Kuroki 2020 Ledwoch 2016 Li W 2022	erences: CI DRT <u>Events</u> 0 3 16 0 2 1 1 6 0 2 2 1 1 6 0 2 2	Total 28 12 61 3 4 2 1 17 19	00. df = 1 non D Events 20 9 126 2 0 0 0 0 11 3 1	RT Total 886 543 1678 423 103 53 94 513 33 151	Weight 11.9% 2.7% 60.7% 0.4% 0.2% 0.2% 0.2% 0.0% 4.2% 2.7% 0.8%	Odds Ratio M-H. Fixed. 95% Cl 0.74 [0.04, 12.57] 19.78 [4.58 84.55] 4.38 [2.41, 7.97] 24.09 [0.97, 598.88] 207.00 [7.75, 5530.42] 107.00 [2.96, 3870.88] 567.00 [8.18, 39307.21] 24.89 [7.80, 79.43] 2.90 [0.10, 85.86] 42.86 [3.46, 531.19]	Odds Ratio
B Study or Subgroup Single-seal Boersma 2017 Della 2021 Dukkipati 2018 Enomoto 2016 Fan Y 2019 Fukunaga 2022 Huang W 2017 Kuroki 2020 Ledwoch 2016 Li W 2022 Reddy 2013 Wiebe 2015	erences: Cr DRT Events 0 3 16 0 2 1 1 6 0 2 1 1 1 6 0 2 1	Total 28 12 61 3 4 2 1 7 1 9 6	00. df = 1 non D Events 20 9 126 2 0 0 0 111 3 1 2	RT Total 886 543 1678 423 103 53 94 513 33 151 136	Weight 11.9% 2.7% 60.7% 0.4% 0.2% 0.2% 0.0% 4.2% 2.7% 0.8% 1.3%	Odds Ratio M-H, Fixed, 95% Cl 0.74 [0.04, 12.57] 19.78 [4.58, 85.45] 4.38 [2.41, 7.97] 24.09 [0.97, 598.88] 207.00 [7.75, 5530.42] 107.00 [2.96, 3870.88] 567.00 [8.18, 39307.21] 24.89 [7.80, 79.43] 2.90 [0.10, 85.86] 42.86 [3.46, 531.19] 13.40 [1.03, 173.53] 7.56 [0.28, 202.09] 7.56 [0.28	Odds Ratio
B Study or Subgroup Single-seal Boersma 2017 Della 2021 Dukkipati 2018 Enomoto 2016 Fan Y 2019 Fukunaga 2022 Huang W 2017 Kuroki 2020 Ledwoch 2016 Li W 2022 Reddy 2013 Wiebe 2015 Subtotal (95% CI)	erences: Cr DRT Events 0 3 16 0 2 1 1 6 0 2 1 1 6 0 2 1 0	Total 28 12 61 3 4 2 1 17 1 9 6 2	20. df = 1 non D Events 20 9 126 2 0 0 0 0 111 3 1 2 2 0 0 0 126 2 0 0 0 126 2 0 0 126 2 0 0 126 2 0 0 126 2 0 0 126 2 0 0 126 2 0 0 126 2 0 0 126 2 0 0 126 2 0 0 126 2 0 0 126 2 0 0 126 2 0 0 0 126 2 0 0 0 126 2 0 0 0 0 126 2 0 0 0 0 0 0 0 0 0 0 0 0 0	RT Total 886 543 1678 423 103 53 94 513 33 151 136 96	Weight 11.9% 2.7% 60.7% 0.2% 0.2% 0.2% 0.0% 4.2% 2.7% 0.8% 1.3% 1.2%	Odds Ratio M-H. Fixed. 95% CI 19.78 [4.58, 85.45] 4.38 [2.41, 7.97] 24.09 [0.97, 598.88] 207.00 [7.75, 5530.42] 107.00 [2.96, 3870.88] 567.00 [8.18, 39307.21] 24.89 [7.80, 79.43] 2.90 [0.10, 85.86] 42.86 [3.46, 531.19] 13.40 [1.03, 173.53]	Odds Ratio
B Study or Subgroup Single-seal Boersma 2017 Della 2021 Dukkipati 2018 Enomoto 2016 Fan Y 2019 Fukunaga 2022 Huang W 2017 Kuroki 2020 Ledwoch 2016 Li W 2022 Reddy 2013 Wiebe 2015	erences: Cr Events 0 3 16 0 2 1 1 6 0 2 1 1 6 0 2 1 1 2 2 1 0 2 2 1 0 2 2 1 0 2 2 1 0 2 2 1 2 2 2 1 2 2 2 1 2 2 2 2 2 2 2 2 2 2 2 2 2	Total 28 12 61 3 4 2 1 17 1 9 6 2 146 11 (P	00. df = 1 non D Events 20 9 126 2 0 0 111 3 1 2 2 176 = 0.010);	RT Total 886 543 1678 423 103 53 94 513 33 151 136 96 4709	Weight 11.9% 2.7% 60.7% 0.4% 0.2% 0.2% 0.0% 4.2% 2.7% 0.8% 1.3% 1.2% 86.4%	Odds Ratio M-H, Fixed, 95% Cl 0.74 [0.04, 12.57] 19.78 [4.58, 85.45] 4.38 [2.41, 7.97] 24.09 [0.97, 598.88] 207.00 [7.75, 5530.42] 107.00 [2.96, 3870.88] 567.00 [8.18, 39307.21] 24.89 [7.80, 79.43] 2.90 [0.10, 85.86] 42.86 [3.46, 531.19] 13.40 [1.03, 173.53] 7.56 [0.28, 202.09] 7.56 [0.28	Odds Ratio
B Study or Subgroup Single-seal Boersma 2017 Della 2021 Dukkipati 2018 Enomoto 2016 Fan Y 2019 Fukunaga 2022 Huang W 2017 Kuroki 2020 Ledwoch 2016 Li W 2022 Reddy 2013 Wiebe 2015 Subtotal (95% CI) Total events Heterogeneity: Chi ² =	erences: Cr Events 0 3 16 0 2 1 1 6 0 2 1 1 6 0 2 1 1 2 2 1 0 2 2 1 0 2 2 1 0 2 2 1 0 2 2 1 2 2 2 1 2 2 2 1 2 2 2 2 2 2 2 2 2 2 2 2 2	Total 28 12 61 3 4 2 1 17 1 9 6 2 146 11 (P	00. df = 1 non D Events 20 9 126 2 0 0 111 3 1 2 2 176 = 0.010);	RT Total 886 543 1678 423 103 53 94 513 33 151 136 96 4709	Weight 11.9% 2.7% 60.7% 0.4% 0.2% 0.2% 0.0% 4.2% 2.7% 0.8% 1.3% 1.2% 86.4%	Odds Ratio M-H, Fixed, 95% Cl 0.74 [0.04, 12.57] 19.78 [4.58, 85.45] 4.38 [2.41, 7.97] 24.09 [0.97, 598.88] 207.00 [7.75, 5530.42] 107.00 [2.96, 3870.88] 567.00 [8.18, 39307.21] 24.89 [7.80, 79.43] 2.90 [0.10, 85.86] 42.86 [3.46, 531.19] 13.40 [1.03, 173.53] 7.56 [0.28, 202.09] 7.56 [0.28	Odds Ratio
B Study or Subgroup Single-seal Boersma 2017 Della 2021 Dukkipati 2018 Enomoto 2016 Fan Y 2019 Fukunaga 2022 Huang W 2017 Kuroki 2020 Ledwoch 2016 Li W 2022 Reddy 2013 Wiebe 2015 Subtotal (95% Cl) Total events Heterogeneity: Chi ² = Test for overall effect:	erences: Cr Events 0 3 16 0 2 1 1 6 0 2 1 1 6 0 2 1 1 2 2 1 0 2 2 1 0 2 2 1 0 2 2 1 0 2 2 1 2 2 2 1 2 2 2 1 2 2 2 2 2 2 2 2 2 2 2 2 2	Total 28 12 61 3 4 2 1 17 1 9 6 2 146 11 (P	00. df = 1 non D Events 20 9 126 2 0 0 111 3 1 2 2 176 = 0.010); 0001)	RT Total 886 543 1678 423 103 53 94 513 33 151 136 96 4709	Weight 11.9% 2.7% 60.7% 0.4% 0.2% 0.2% 0.0% 4.2% 2.7% 0.8% 1.3% 1.2% 86.4%	Odds Ratio M-H. Fixed. 95% Cl 0.74 [0.04, 12.57] 19.78 [4.58, 85.45] 4.38 [2.41, 7.97] 24.09 [0.97, 598.88] 207.00 [7.75, 5530.42] 107.00 [2.96, 3870.88] 567.00 [8.18, 39307.21] 24.89 [7.80, 79.43] 2.90 [0.10, 85.86] 42.86 [3.46, 531.19] 13.40 [1.03, 173.53] 7.56 [0.28, 202.09] 7.06 [4.67, 10.67]	Odds Ratio
B Study or Subgroup Single-seal Boersma 2017 Della 2021 Dukkipati 2018 Enomoto 2016 Fan Y 2019 Fukunaga 2022 Huang W 2017 Kuroki 2020 Ledwoch 2016 Li W 2022 Reddy 2013 Wiebe 2015 Subtotal (95% CI) Total events Heterogeneity: Chi ² = Test for overall effect: Dual-seal Aminian 2019	PRT Events 0 3 16 0 2 1 1 6 0 2 1 1 0 2 2 4.73, df = Z = 9.27 (f Z 2	Total 28 12 61 3 4 2 1 17 1 9 6 2 2 146 11 (P C < 0.0 9	00. df = 1 non D Events 20 9 126 2 0 0 0 0 111 3 11 2 2 176 = 0.010); 0001) 32	RT Total 8866 543 1678 423 103 53 94 513 33 151 136 96 4709 ² = 56' 1079	Weight 11.9% 2.7% 60.7% 0.4% 0.2% 0.2% 0.2% 0.2% 0.2% 0.8% 1.3% 1.2% 86.4% % 3.8%	Odds Ratio M-H. Fixed. 95% CI 0.74 [0.04, 12.57] 19.78 [4.58, 85.45] 4.38 [2.41, 7.97] 24.09 [0.97, 598.88] 207.00 [7.75, 5530.42] 107.00 [2.96, 3870.88] 567.00 [8.18, 39307.21] 24.89 [7.80, 79.43] 2.90 [0.10, 85.86] 42.86 [3.46, 531.19] 13.40 [1.03, 173.53] 7.56 [0.28, 202.09] 7.06 [4.67, 10.67] 9.35 [1.87, 46.78]	Odds Ratio
B Study or Subgroup Single-seal Boersma 2017 Della 2021 Dukkipati 2018 Enomoto 2016 Fan Y 2019 Fukunaga 2022 Huang W 2017 Kuroki 2020 Ledwoch 2016 Li W 2022 Reddy 2013 Wiebe 2015 Subtotal (95% CI) Total events Heterogeneity: Chi ² = Test for overall effect: Dual-seal Aminian 2019 Huang H 2017	DRT Events 0 3 16 0 2 1 6 0 2 1 6 2 1 6 2 1 2 2 2 2 2 0 32 2 2 0	Total 28 12 61 3 4 2 1 7 1 9 6 2 146 11 (P 2 < 0.0 9 2	00. df = 1 non D Events 20 9 126 2 0 0 0 111 3 1 2 2 176 = 0.010); 0001) 32 2 2	RT Total 8866 543 1678 423 103 53 94 513 33 31 511 136 96 4709 ² = 56 ^o 1079 119	Weight 11.9% 2.7% 0.4% 0.2% 0.2% 0.2% 0.8% 1.3% 1.2% 86.4% % 3.8% 0.9%	Odds Ratio M-H. Fixed. 95% Cl 0.74 [0.04, 12.57] 19.78 [4.58, 85.45] 4.38 [2.41, 7.97] 24.09 [0.97, 598.88] 207.00 [7.75, 553.042] 107.00 [2.96, 3870.88] 567.00 [8.18, 39307.21] 24.89 [7.80, 79.43] 2.90 [0.10, 85.86] 42.86 [3.46, 531.19] 13.40 [1.03, 173.53] 7.56 [0.28, 202.09] 7.06 [4.67, 10.67] 9.35 [1.87, 46.78] 9.40 [0.35, 250.97]	Odds Ratio
B Study or Subgroup Single-seal Boersma 2017 Della 2021 Dukkipati 2018 Enomoto 2016 Fan Y 2019 Fukunaga 2022 Huang W 2017 Kuroki 2020 Ledwoch 2016 Li W 2022 Reddy 2013 Wiebe 2015 Subtotal (95% Cl) Total events Heterogeneity: Chi ² = Test for overall effect: Dual-seal Aminian 2019 Huang H 2017 Kebernik 2015	DRT Events 0 3 16 0 2 1 6 0 2 1 6 2 1 6 2 1 2 2 2 2 2 2 2 0 32 2 2 0 32 2 0 32 2 1 0 32 2 0 2 0 1	Total 28 12 61 3 4 2 1 17 1 9 6 2 2 146 11 (P 2 < 0.0 9 2 1	00. df = 1 non D Events 20 9 126 2 0 0 111 3 1 2 2 176 = 0.010); 0001) 322 2 1	RT Total 886 543 1678 423 103 53 94 513 33 151 136 4709 1 ² = 56 ⁴ 1079 119 88	Weight 11.9% 2.7% 60.7% 0.4% 0.2% 0.0% 4.2% 2.7% 0.8% 1.3% 86.4% % 3.8% 0.9% 0.2%	Odds Ratio M-H. Fixed. 95% Cl 0.74 [0.04, 12.57] 19.78 [4.58, 85.45] 4.38 [2.41, 7.97] 24.09 [0.97, 598.88] 207.00 [7.75, 5530.42] 107.00 [2.96, 3870.88] 567.00 [8.18, 39307.21] 24.89 [7.80, 79.43] 2.90 [0.10, 85.86] 42.86 [3.46, 531.19] 13.40 [1.03, 173.53] 7.56 [0.28, 202.09] 7.06 [4.67, 10.67] 9.40 [0.35, 250.97] 175.00 [4.86, 6306.29]	Odds Ratio
B Study or Subgroup Single-seal Boersma 2017 Della 2021 Dukkipati 2018 Enomoto 2016 Fan Y 2019 Fukunaga 2022 Huang W 2017 Kuroki 2020 Ledwoch 2016 Li W 2022 Reddy 2013 Wiebe 2015 Subtotal (95% CI) Total events Heterogeneity: Chi ² = Test for overall effect: Dual-seal Aminian 2019 Huang H 2017 Kebernik 2015 Saw 2017	DRT Events 0 3 16 0 2 1 6 0 2 1 6 2 1 2 24.73, df = Z = 9.27 (f 2 0 1 0	Total 28 12 61 3 4 2 11 17 19 6 2 2 146 11 (P 2 < 0.0 9 2 2 1 11	00. df = 1 non D Events 20 9 126 2 0 0 0 11 3 1 2 2 176 = 0.010); 0001) 322 2 17 7	RT Total 886 543 1678 423 103 53 94 513 33 151 136 96 4709 1 ² = 56 ^r 1079 119 88 328	Weight 11.9% 2.7% 60.7% 0.4% 0.2% 0.0% 4.2% 2.7% 0.8% 1.2% 86.4% % 3.8% 0.9% 0.2% 4.7%	Odds Ratio M-H. Fixed. 95% Cl 0.74 [0.04, 12.57] 19.78 [4.58, 85.45] 4.38 [2.41, 7.97] 24.09 [0.97, 598.88] 207 00 [7.75, 5530 42] 107.00 [2.96, 38307.21] 24.89 [7.80, 79.43] 2.90 [0.10, 85.86] 42.86 [3.46, 531.19] 13.40 [1.03, 173.53] 7.56 [0.28, 202.09] 7.06 [4.67, 10.67] 9.40 [0.35, 250.97] 175.00 [4.86, 6306.29] 1.86 [0.10, 34.64]	Odds Ratio
B Study or Subgroup Single-seal Boersma 2017 Della 2021 Dukkipati 2018 Enomoto 2016 Fan Y 2019 Fukunaga 2022 Huang W 2017 Kuroki 2020 Ledwoch 2016 Li W 2022 Reddy 2013 Wiebe 2015 Subtotal (95% CI) Total events Heterogeneity: Chi ² = Test for overall effect: Dual-seal Aminian 2019 Huang H 2017 Kebernik 2015 Saw 2017 Szymala 2017	DRT Events 0 3 16 0 2 11 6 0 2 1 6 2 1 6 2 1 6 2 1 0 2 2 2 0 2 0 1 0	Total 28 12 61 3 4 2 11 9 2 9 2 11 9 2 11 5	00. df = 1 non D Events 20 9 126 2 0 0 126 2 0 0 0 111 3 1 2 2 176 = 0.010); 0001) 32 2 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 7 1 7 7 1 7 7 1 7 7 7 7 7 7 7 7 7 7 7 7 7	RT Total 886 543 1678 423 103 53 94 513 33 151 136 96 4709 1 ² = 56 ^o 1079 119 88 8328 72	Weight 11.9% 2.7% 60.7% 0.2% 0.2% 0.2% 4.2% 2.7% 0.8% 1.2% 86.4% % 3.8% 0.9% 0.9% 0.2% 4.7% 1.9%	Odds Ratio M-H. Fixed. 95% CI 0.74 [0.04, 12.57] 19.78 [4.58, 85.45] 4.38 [2.41, 7.97] 24.09 [0.97, 598.88] 207.00 [7.75, 5530.42] 107.00 [2.96, 3870.88] 567.00 [8.18, 39307.21] 24.89 [7.80, 79.43] 2.90 [0.10, 85.86] 42.86 [3.46, 531.19] 13.40 [1.03, 173.53] 7.56 [0.28, 202.09] 7.06 [4.67, 10.67] 9.35 [1.87, 46.78] 9.40 [0.35, 250.97] 175.00 [4.86, 6306.29] 1.86 [0.10, 34.64] 4.33 [0.16, 119.39]	Odds Ratio
B Study or Subgroup Single-seal Boersma 2017 Della 2021 Dukkipati 2018 Enomoto 2016 Fan Y 2019 Fukunaga 2022 Huang W 2017 Kuroki 2020 Ledwoch 2016 Li W 2022 Reddy 2013 Wiebe 2015 Subtotal (95% CI) Total events Heterogeneity: Chi ² = Test for overall effect: Dual-seal Aminian 2019 Huang H 2017 Kebernik 2015 Saw 2017 Szymala 2017	DRT Events 0 3 16 0 2 1 6 0 2 1 6 2 1 2 24.73, df = Z = 9.27 (f 2 0 1 0	Total 288 122 611 3 4 2 61 3 4 2 11 7 1 9 6 6 2 146 11 (P 2 4 4 6 1 3 4 2 146 9 2 146 9 2 1 1 15 5 12	00. df = 1 non D Events 20 9 126 2 0 0 0 11 3 1 2 2 176 = 0.010); 0001) 322 2 17 7	RT Total 8866 543 103 53 94 423 103 53 94 4709 113 6 4709 119 88 8328 328 72 157	Weight 11.9% 2.7% 60.7% 0.4% 0.2% 4.2% 2.7% 0.8% 1.3% 86.4% % 3.8% 0.9% 0.2% 4.7% 1.9% 2.0%	Odds Ratio M-H. Fixed. 95% CI 0.74 [0.04, 12.57] 19.78 [4.58, 85.45] 4.38 [2.41, 7.97] 24.09 [0.97, 598.88] 207.00 [7.75, 553.042] 107.00 [2.96, 3870.88] 567.00 [8.18, 39307.21] 24.89 [7.80, 79.43] 2.90 [0.10, 85.86] 42.86 [3.46, 531.19] 13.40 [1.03, 173.53] 7.56 [0.28, 202.09] 7.06 [4.67, 10.67] 9.40 [0.35, 250.97] 175.00 [4.86, 6306.29] 1.86 [0.10, 30, 464] 4.33 [0.16, 119.39] 4.17 [0.16, 107.85]	Odds Ratio
B Study or Subgroup Single-seal Boersma 2017 Della 2021 Dukkipati 2018 Enomoto 2016 Fan Y 2019 Fukunaga 2022 Huang W 2017 Kuroki 2020 Ledwoch 2016 Li W 2022 Reddy 2013 Wiebe 2015 Subtotal (95% CI) Total events Heterogeneity: Chi ² = Test for overall effect: Dual-seal Aminian 2019 Huang H 2017 Kebernik 2015 Saw 2017 Szymala 2017	DRT Events 0 3 16 0 2 11 6 0 2 1 6 2 1 6 2 1 6 2 1 0 2 2 2 0 2 0 1 0	Total 28 12 61 3 4 2 11 9 2 9 2 11 9 2 11 5	00. df = 1 non D Events 20 9 126 2 0 0 126 2 0 0 0 111 3 1 2 2 176 = 0.010); 0001) 32 2 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 7 1 7 7 1 7 7 1 7 7 7 7 7 7 7 7 7 7 7 7 7	RT Total 886 543 1678 423 103 53 94 513 33 151 136 96 4709 1 ² = 56 ^o 1079 119 88 8328 72	Weight 11.9% 2.7% 60.7% 0.2% 0.2% 0.2% 4.2% 2.7% 0.8% 1.2% 86.4% % 3.8% 0.9% 0.9% 0.2% 4.7% 1.9%	Odds Ratio M-H. Fixed. 95% CI 0.74 [0.04, 12.57] 19.78 [4.58, 85.45] 4.38 [2.41, 7.97] 24.09 [0.97, 598.88] 207.00 [7.75, 5530.42] 107.00 [2.96, 3870.88] 567.00 [8.18, 39307.21] 24.89 [7.80, 79.43] 2.90 [0.10, 85.86] 42.86 [3.46, 531.19] 13.40 [1.03, 173.53] 7.56 [0.28, 202.09] 7.06 [4.67, 10.67] 9.35 [1.87, 46.78] 9.40 [0.35, 250.97] 175.00 [4.86, 6306.29] 1.86 [0.10, 34.64] 4.33 [0.16, 119.39]	Odds Ratio
B Study or Subgroup Single-seal Boersma 2017 Della 2021 Dukkipati 2018 Enomoto 2016 Fan Y 2019 Fukunaga 2022 Huang W 2017 Kuroki 2020 Ledwoch 2016 Li W 2022 Reddy 2013 Wiebe 2015 Subtotal (95% CI) Total events Heterogeneity: Chi ² = Test for overall effect: Dual-seal Aminian 2019 Huang H 2017 Kebernik 2015 Saw 2017 Szymala 2017	DRT Events 0 3 16 0 2 11 6 0 2 1 6 2 1 6 2 1 6 2 1 0 2 2 2 0 2 0 1 0	Total 288 122 611 3 4 2 61 3 4 2 11 7 1 9 6 6 2 146 11 (P 2 4 4 6 1 3 4 2 146 9 2 146 9 2 1 1 15 5 12	00. df = 1 non D Events 20 9 126 2 0 0 126 2 0 0 0 111 3 1 2 2 176 = 0.010); 0001) 32 2 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7 7 1 7 7 1 7 7 1 7 7 7 7 7 7 7 7 7 7 7 7 7	RT Total 8866 543 103 53 94 423 103 53 94 4709 113 6 4709 119 88 8328 328 72 157	Weight 11.9% 2.7% 60.7% 0.4% 0.2% 4.2% 2.7% 0.8% 1.3% 86.4% % 3.8% 0.9% 0.2% 4.7% 1.9% 2.0%	Odds Ratio M-H. Fixed. 95% CI 0.74 [0.04, 12.57] 19.78 [4.58, 85.45] 4.38 [2.41, 7.97] 24.09 [0.97, 598.88] 207.00 [7.75, 553.042] 107.00 [2.96, 3870.88] 567.00 [8.18, 39307.21] 24.89 [7.80, 79.43] 2.90 [0.10, 85.86] 42.86 [3.46, 531.19] 13.40 [1.03, 173.53] 7.56 [0.28, 202.09] 7.06 [4.67, 10.67] 9.40 [0.35, 250.97] 175.00 [4.86, 6306.29] 1.86 [0.10, 30, 464] 4.33 [0.16, 119.39] 4.17 [0.16, 107.85]	Odds Ratio
B Study or Subgroup Single-seal Boersma 2017 Della 2021 Dukkipati 2018 Enomoto 2016 Fan Y 2019 Fukunaga 2022 Huang W 2017 Kuroki 2020 Ledwoch 2016 Li W 2022 Reddy 2013 Wiebe 2015 Subtotal (95% Cl) Total events Heterogeneity: Chi ² = Test for overall effect: Dual-seal Aminian 2019 Huang H 2017 Kebernik 2015 Saw 2017 Szymala 2017 Woffrum 2016 Subtotal (95% Cl)	PRT Events 0 3 16 0 2 1 1 6 0 2 2 1 1 0 2 2 4.73, df = 5 2 0 1 0 0 2 2 4.20, df = 5 2 4.20, df = 5	$\begin{array}{c} \textbf{Total} \\ \textbf{Total} \\ \textbf{28} \\ \textbf{12} \\ \textbf{61} \\ \textbf{3} \\ \textbf{4} \\ \textbf{28} \\ \textbf{12} \\ \textbf{61} \\ \textbf{3} \\ \textbf{4} \\ \textbf{2} \\ \textbf{11} \\ \textbf{7} \\ \textbf{1} \\ \textbf{9} \\ \textbf{6} \\ \textbf{2} \\ \textbf{11} \\ \textbf{7} \\ \textbf{10} \\ \textbf{9} \\ \textbf{9} \\ \textbf{2} \\ \textbf{11} \\ \textbf{11} \\ \textbf{5} \\ \textbf{12} \\ \textbf{40} \end{array}$	00. df = 1 non D Events 20 9 126 2 0 0 126 2 0 0 0 0 111 3 1 2 2 176 = 0.010); 0001) 32 2 1 176 1 1 4 4 2 2 176 1 1 1 1 1 1 1 1 1 1 1 1 1	RT Total 8866 543 1678 423 103 53 394 513 33 151 1366 96 4709 1 ² = 56 ⁴ 1079 1 ¹⁹ 88 328 72 157 1843	Weight 11.9% 2.7% 60.7% 0.4% 0.2% 4.2% 2.7% 0.8% 1.3% 86.4% % 3.8% 0.9% 0.2% 4.7% 1.9% 2.0%	Odds Ratio M-H. Fixed. 95% CI 0.74 [0.04, 12.57] 19.78 [4.58, 85.45] 4.38 [2.41, 7.97] 24.09 [0.97, 598.88] 207.00 [7.75, 553.042] 107.00 [2.96, 3870.88] 567.00 [8.18, 39307.21] 24.89 [7.80, 79.43] 2.90 [0.10, 85.86] 42.86 [3.46, 531.19] 13.40 [1.03, 173.53] 7.56 [0.28, 202.09] 7.06 [4.67, 10.67] 9.40 [0.35, 250.97] 175.00 [4.86, 6306.29] 1.86 [0.10, 30, 464] 4.33 [0.16, 119.39] 4.17 [0.16, 107.85]	Odds Ratio
B Study or Subgroup Single-seal Boersma 2017 Della 2021 Dukkipati 2018 Enomoto 2016 Fan Y 2019 Fukunaga 2022 Huang W 2017 Kuroki 2020 Ledwoch 2016 Li W 2022 Reddy 2013 Wiebe 2015 Subtotal (95% Cl) Total events Heterogeneity: Chi ² = Test for overall effect: Dual-seal Aminian 2019 Huang H 2017 Kebernik 2015 Saw 2017 Szymala 2017 Wolfrum 2016 Subtotal (95% Cl) Total events Heterogeneity: Chi ² = Test for overall effect:	PRT Events 0 3 16 0 2 1 1 6 0 2 2 1 1 0 2 2 4.73, df = 5 2 0 1 0 0 2 2 4.20, df = 5 2 4.20, df = 5	$\begin{array}{c} \textbf{Total} \\ \textbf{Total} \\ \textbf{28} \\ \textbf{12} \\ \textbf{61} \\ \textbf{3} \\ \textbf{4} \\ \textbf{28} \\ \textbf{12} \\ \textbf{61} \\ \textbf{3} \\ \textbf{4} \\ \textbf{2} \\ \textbf{11} \\ \textbf{7} \\ \textbf{1} \\ \textbf{9} \\ \textbf{6} \\ \textbf{2} \\ \textbf{11} \\ \textbf{7} \\ \textbf{10} \\ \textbf{9} \\ \textbf{9} \\ \textbf{2} \\ \textbf{11} \\ \textbf{11} \\ \textbf{5} \\ \textbf{12} \\ \textbf{40} \end{array}$	00. df = 1 non D Events 20 9 126 2 0 0 126 2 0 0 0 0 111 3 1 2 2 176 = 0.010); 0001) 32 2 1 176 1 1 4 4 2 2 176 1 1 1 1 1 1 1 1 1 1 1 1 1	RT Total 886 543 1678 423 103 53 394 513 33 151 136 96 4709 12° = 56° 1079 119 88 328 72 157 1843 0%	Weight 11.9% 2.7% 60.7% 0.4% 0.2% 0.0% 4.2% 2.7% 0.8% 1.3% 86.4% % 3.8% 0.9% 0.2% 4.7% 1.9% 2.0% 13.6%	Odds Ratio M-H, Fixed, 95% Cl 0.74 [0.04, 12.57] 19.78 [4.58, 85.45] 4.38 [2.41, 7.97] 24.09 [0.97, 598.88] 207.00 [7.75, 5530.42] 107.00 [2.96, 3670.88] 567.00 [8.18, 39307.21] 24.89 [7.80, 79.43] 2.90 [0.10, 85.86] 42.86 [3.46, 531.19] 13.40 [1.03, 173.53] 7.56 [0.28, 202.09] 7.06 [4.67, 10.67] 9.40 [0.35, 250.97] 175.00 [4.86, 6306.29] 1.86 [0.10, 34.64] 4.33 [0.16, 119.39] 4.17 [0.16, 107.85] 7.14 [2.68, 19.03]	Odds Ratio
B Study or Subgroup Single-seal Boersma 2017 Della 2021 Dukkipati 2018 Enomoto 2016 Fan Y 2019 Fukunaga 2022 Huang W 2017 Kuroki 2020 Ledwoch 2016 Li W 2022 Reddy 2013 Wiebe 2015 Subtotal (95% CI) Total events Heterogeneity: Chi ² = Test for overall effect: Dual-seal Aminian 2019 Huang H 2017 Kebernik 2015 Saw 2017 Szymala 2017 Wolfrum 2016 Subtotal (95% CI) Total events Heterogeneity: Chi ² = Test for overall effect: Total (95% CI)	PRT Events 0 3 16 0 2 1 1 6 0 2 1 1 6 0 2 2 4.73, df = 5 2 0 3 2 2.4.73, df = 5 2 0 3 2 2.4.73, df = 5 2 0 1 0 3 2 2 1 0 3 2 2 1 0 3 2 2 2 2 4 5 2 2 1 1 0 3 2 2 1 1 0 3 2 2 1 1 0 3 2 2 1 1 0 3 2 2 1 1 0 3 2 2 1 1 0 3 2 2 2 7 (F 2 2 7 (F 2 2 2 7 (F 2 2 2 2 7 (F 2 2 2 7 (F 2 2 2 2 7 (F 2 2 2 2 3 2 2 2 7 (F 2 2 2 3 2 2 3 2 2 2 3 2 2 3 2 2 3 2 2 3 2 2 3 2 2 3 2 2 3 2 2 3 2 2 3 2 2 3 3 2 2 3 2 2 3 2 2 3 3 2 2 3 2 2 3 3 2 2 3 3 2 2 3 3 2 2 3 3 2 2 3 3 3 2 2 3 3 3 2 2 3 3 3 2 2 3 3 3 3 3 3 2 2 3 3 3 3 3 3 3 3 3 3 3 3 3	$\begin{array}{c} {\rm Total} \\ \\ {\rm 288} \\ {\rm 12} \\ {\rm 28} \\ {\rm 12} \\ {\rm 61} \\ {\rm 3} \\ {\rm 4} \\ {\rm 2} \\ {\rm 11} \\ {\rm 177} \\ {\rm 1} \\ {\rm 99} \\ {\rm 6} \\ {\rm 2} \\ {\rm 116} \\ {\rm 110} \\ {\rm 100} \\ {\rm $	00. df = 1 non D Events 20 9 126 2 0 0 111 3 1 2 2 176 = 0.010); 0001) 322 2 177 1 1 44 0.52); l ² = 001)	RT Total 886 543 1678 423 103 53 394 513 33 151 136 96 4709 12° = 56° 1079 119 88 328 72 157 1843 0%	Weight 11.9% 2.7% 60.7% 0.4% 0.2% 4.2% 2.7% 0.8% 1.3% 86.4% % 3.8% 0.9% 0.2% 4.7% 1.9% 2.0%	Odds Ratio M-H. Fixed. 95% CI 0.74 [0.04, 12.57] 19.78 [4.58, 85.45] 4.38 [2.41, 7.97] 24.09 [0.97, 598.88] 207.00 [7.75, 553.042] 107.00 [2.96, 3870.88] 567.00 [8.18, 39307.21] 24.89 [7.80, 79.43] 2.90 [0.10, 85.86] 42.86 [3.46, 531.19] 13.40 [1.03, 173.53] 7.56 [0.28, 202.09] 7.06 [4.67, 10.67] 9.40 [0.35, 250.97] 175.00 [4.86, 6306.29] 1.86 [0.10, 30, 46.4] 4.33 [0.16, 119.39] 4.17 [0.16, 107.85]	Odds Ratio
B Study or Subgroup Single-seal Boersma 2017 Della 2021 Dukkipati 2018 Enomoto 2016 Fan Y 2019 Fukunaga 2022 Huang W 2017 Kuroki 2020 Ledwoch 2016 Li W 2022 Reddy 2013 Wiebe 2015 Subtotal (95% CI) Total events Heterogeneity: Chi ² = Test for overall effect: Dual-seal Aminian 2019 Huang H 2017 Kebernik 2015 Saw 2017 Szymala 2017 Szymala 2017 Volfrum 2016 Subtotal (95% CI) Total events Heterogeneity: Chi ² = Test for overall effect: Total (95% CI)	PRT Events 0 3 16 0 2 1 1 6 0 2 1 1 0 2 2 4.20, df = { 2 0 3 4.20, df = { 2 3 3 5 3 5 3 5 3 5 3 5 3 5 3 5 3 5 3 5 3 5 3 5 3 5 3 5 5 5 5 5 5 5 5 5 5 5 5 5	$\begin{array}{c} \textbf{Total} \\ \textbf{Total} \\ \textbf{28} \\ \textbf{12} \\ \textbf{61} \\ \textbf{3} \\ \textbf{42} \\ \textbf{61} \\ \textbf{3} \\ \textbf{42} \\ \textbf{11} \\ \textbf{7} \\ \textbf{146} \\ \textbf{11} \\ \textbf{9} \\ \textbf{6} \\ \textbf{22} \\ \textbf{146} \\ \textbf{11} \\ \textbf{11} \\ \textbf{5} \\ \textbf{122} \\ \textbf{40} \\ \textbf{6} \\ \textbf{(P = (C_{1})^{2} < 0.0)} \\ \textbf{186} \end{array}$	00. df = 1 non D Events 20 9 126 2 0 0 126 2 0 0 0 111 3 1 2 2 176 = 0.010); 0001) 32 2 177 1 1 44 0.52); I ² = 001) 220	RT Total 8866 543 103 53 33 151 136 9 4709 12 = 56' 1079 119 88 328 72 157 1843 0% 6552	Weight 11.9% 2.7% 60.7% 0.4% 0.2% 0.2% 2.7% 0.8% 1.2% 86.4% 3.8% 0.9% 0.2% 4.7% 1.9% 2.0% 1.9% 2.0% 1.3.6%	Odds Ratio M-H, Fixed, 95% Cl 0.74 [0.04, 12.57] 19.78 [4.58, 85.45] 4.38 [2.41, 7.97] 24.09 [0.97, 598.88] 207.00 [7.75, 5530.42] 107.00 [2.96, 3670.88] 567.00 [8.18, 39307.21] 24.89 [7.80, 79.43] 2.90 [0.10, 85.86] 42.86 [3.46, 531.19] 13.40 [1.03, 173.53] 7.56 [0.28, 202.09] 7.06 [4.67, 10.67] 9.40 [0.35, 250.97] 175.00 [4.86, 6306.29] 1.86 [0.10, 34.64] 4.33 [0.16, 119.39] 4.17 [0.16, 107.85] 7.14 [2.68, 19.03]	Odds Ratio M-H. Fixed. 95% CI
B Study or Subgroup Single-seal Boersma 2017 Della 2021 Dukkipati 2018 Enomoto 2016 Fan Y 2019 Fukunaga 2022 Huang W 2017 Kuroki 2020 Ledwoch 2016 Li W 2022 Reddy 2013 Wiebe 2015 Subtotal (95% CI) Total events Heterogeneity: Chi ² = Test for overall effect: Dual-seal Aminian 2019 Huang H 2017 Kebernik 2015 Saw 2017 Szymala 2017 Wolfrum 2016 Subtotal (95% CI) Total events Heterogeneity: Chi ² = Test for overall effect: Total (95% CI)	PRT Events 0 3 16 0 3 16 0 2 1 1 1 6 0 2 1 1 1 6 0 2 1 1 2 2 4.73, df = { 2 0 3 2 2 4.73, df = { 2 0 3 2 2 4.73, df = { 2 0 3 2 2 1 1 0 2 2 1 1 0 2 2 1 1 0 2 2 1 1 0 2 2 1 1 0 2 2 1 1 0 2 2 1 1 0 2 2 1 1 0 2 2 1 0 0 2 2 1 0 0 2 2 1 0 0 2 2 1 0 0 2 2 1 0 0 2 2 1 0 0 2 2 1 0 0 2 2 1 0 0 2 2 1 0 0 2 2 1 0 0 2 2 1 0 0 2 2 1 0 0 2 2 1 0 0 2 2 1 0 0 2 2 1 0 0 2 2 1 0 2 2 0 2 7 (F - 2 0 2 0 1 0 0 2 2 0 2 7 (F - 2 0 2 0 1 0 0 0 0 0 0 0 0 0 0 0 0 0	$\begin{array}{c} \text{Total} \\ \hline \\ 28 \\ 12 \\ 61 \\ 3 \\ 4 \\ 2 \\ 11 \\ 17 \\ 1 \\ 9 \\ 6 \\ 2 \\ 146 \\ 11 (P \\ 0.0 \\ 9 \\ 2 \\ 1 \\ 11 \\ 5 \\ 12 \\ 40 \\ 186 \\ 17 (P \\ 17 (P \\ 10 \\ 10 \\ 10 \\ 10 \\ 10 \\ 10 \\ 10 \\ 1$	00. df = 1 non D Events 20 9 126 2 0 0 111 3 1 2 2 176 = 0.010); 0001) 322 2 1 7 1 1 44 0.52); ² = 001) 2200 = 0.04); ²	RT Total 8866 543 103 53 33 151 136 9 4709 12 = 56' 1079 119 88 328 72 157 1843 0% 6552	Weight 11.9% 2.7% 60.7% 0.4% 0.2% 0.2% 2.7% 0.8% 1.2% 86.4% 3.8% 0.9% 0.2% 4.7% 1.9% 2.0% 1.9% 2.0% 1.3.6%	Odds Ratio M-H, Fixed, 95% Cl 0.74 [0.04, 12.57] 19.78 [4.58, 85.45] 4.38 [2.41, 7.97] 24.09 [0.97, 598.88] 207.00 [7.75, 5530.42] 107.00 [2.96, 3670.88] 567.00 [8.18, 39307.21] 24.89 [7.80, 79.43] 2.90 [0.10, 85.86] 42.86 [3.46, 531.19] 13.40 [1.03, 173.53] 7.56 [0.28, 202.09] 7.06 [4.67, 10.67] 9.40 [0.35, 250.97] 175.00 [4.86, 6306.29] 1.86 [0.10, 34.64] 4.33 [0.16, 119.39] 4.17 [0.16, 107.85] 7.14 [2.68, 19.03]	Odds Ratio

FIGURE 5

Forest plots of stroke (A) and systemic embolism (SE) (B) in device related thrombus (DRT) and non-DRT patients with subgroup analysis based on occlusion mechanism.

09

				Risk Ratio			Risk Ratio		
Study or Subgroup	log[Risk Ratio]		-	IV, Random, 95% CI		<u>IV, Ra</u>	andom, 959	% Cl	
Aminian 2019		0.0342		1.08 [1.01, 1.15]		_			
Li W 2022	-0.033	0.066		0.97 [0.85, 1.10]					
Saw 2017	-0.02	0.038	37.8%	0.98 [0.91, 1.06]			1		
Total (95% Cl)			100.0%	1.02 [0.94, 1.10]			+		
Heterogeneity: Tau ² = Test for overall effect:			= 0.11); F	2 = 55%	0.5	0.7	1	1.5	2
В				Risk Ratio		R	isk Ratio		
Study or Subgroup	log[Risk Ratio]	SE	Weight	IV, Random, 95% Cl			<u>ndom, 95%</u>	6 CI	
Aminian 2019	0.344	0.508	17.5%	1.41 [0.52, 3.82]		-			
Dukkipati 2018	0.588	0.115	72.5%	1.80 [1.44, 2.26]			📲		
Li W 2022	-0.251	0.958	5.8%	0.78 [0.12, 5.09]	-		•		
Zhang X 2021	2.4495	1.131	4.2%	11.58 [1.26, 106.30]					. →
Total (95% CI)			100.0%	1.78 [1.12, 2.83]				•	
Heterogeneity: Tau ² =	0.06; Chi² = 3.70.	df = 3 (F	P = 0.30);	2 = 19%				<u> </u>	
Test for overall effect:					0.05	0.2	1	5	20
с				Risk Ratio		F	Risk Ratio		
Study or Subgroup	log[Risk Ratio]	SE	Weight	IV, Random, 95% CI		<u>IV, Ra</u>	andom, 95º	% CI	
Dukkipati 2018	-0.329	0.137	46.7%	0.72 [0.55, 0.94]					
Li W 2022	-1.0847	1.1718	20.9%	0.34 [0.03, 3.36]					
Saw 2017	4 00 40	0 7404	00 40/						
Can 2011	1.6042	0.7104	32.4%	4.97 [1.24, 20.02]					
Total (95% CI)	1.6042	0.7104	32.4%	4.97 [1.24, 20.02] 1.15 [0.28, 4.68]		-			
Total (95% CI) Heterogeneity: Tau² =	1.08; Chi² = 7.63, c	lf = 2 (P	100.0%	1.15 [0.28, 4.68]	 0.005	0.1			200
Total (95% CI) Heterogeneity: Tau ² = Test for overall effect:	1.08; Chi² = 7.63, c	lf = 2 (P	100.0%	1.15 [0.28, 4.68]	 0.005	0.1		10	200
Total (95% CI) Heterogeneity: Tau² =	1.08; Chi² = 7.63, c	lf = 2 (P	100.0%	1.15 [0.28, 4.68]	- 0.005		1 Risk Ratio	10	 _ 200
Total (95% CI) Heterogeneity: Tau ² = Test for overall effect:	1.08; Chi² = 7.63, c	∄f = 2 (P	100.0% = 0.02); F	1.15 [0.28, 4.68] ² = 74%		F	1 Risk Ratio		200
Total (95% CI) Heterogeneity: Tau ² = Test for overall effect: D	1.08; Chi² = 7.63, c Z = 0.19 (P = 0.85)	ff = 2 (P SE	100.0% = 0.02); F	1.15 [0.28, 4.68] ² = 74% Risk Ratio		F			200
Total (95% Cl) Heterogeneity: Tau ² = Test for overall effect: D Study or Subgroup	1.08; Chi² = 7.63, c Z = 0.19 (P = 0.85) log[Risk Ratio]	lf = 2 (P <u>SE</u> 0.6372	100.0% = 0.02); F <u>Weight</u>	1.15 [0.28, 4.68] ² = 74% Risk Ratio IV, Random, 95% Cl		F			200
Total (95% CI) Heterogeneity: Tau ² = Test for overall effect: D <u>Study or Subgroup</u> Aminian 2019	1.08; Chi ² = 7.63, c Z = 0.19 (P = 0.85) <u>log[Risk Ratio]</u> -0.0943 0.3067	lf = 2 (P <u>SE</u> 0.6372	100.0% = 0.02); F <u>Weight</u> 40.8% 23.3%	1.15 [0.28, 4.68] ² = 74% Risk Ratio <u>IV, Random, 95% CI</u> 0.91 [0.26, 3.17]		F			200
Total (95% CI) Heterogeneity: Tau ² = Test for overall effect: D <u>Study or Subgroup</u> Aminian 2019 Li W 2022	1.08; Chi ² = 7.63, c Z = 0.19 (P = 0.85) <u>log[Risk Ratio]</u> -0.0943 0.3067	ff = 2 (P <u>SE</u> 0.6372 0.8438	100.0% = 0.02); F <u>Weight</u> 40.8% 23.3%	1.15 [0.28, 4.68] ² = 74% Risk Ratio IV, Random, 95% CI 0.91 [0.26, 3.17] 1.36 [0.26, 7.10]		F			200
Total (95% CI) Heterogeneity: Tau ² = Test for overall effect: D Study or Subgroup Aminian 2019 Li W 2022 Saw 2017	1.08; Chi ² = 7.63, c Z = 0.19 (P = 0.85) <u>log[Risk Ratio]</u> -0.0943 0.3067 0.802 0.00; Chi ² = 0.93, c	ff = 2 (P <u>SE</u> 0.6372 0.8438 0.6784 ff = 2 (P	100.0% = 0.02); F <u>Weight</u> 40.8% 23.3% 36.0% 100.0%	1.15 [0.28, 4.68] ² = 74% Risk Ratio <u>IV, Random, 95% CI</u> 0.91 [0.26, 3.17] 1.36 [0.26, 7.10] 2.23 [0.59, 8.43] 1.38 [0.62, 3.06]		F			200
Total (95% CI) Heterogeneity: Tau ² = Test for overall effect: D Study or Subgroup Aminian 2019 Li W 2022 Saw 2017 Total (95% CI) Heterogeneity: Tau ² = Test for overall effect:	1.08; Chi ² = 7.63, c Z = 0.19 (P = 0.85) <u>log[Risk Ratio]</u> -0.0943 0.3067 0.802 0.00; Chi ² = 0.93, c	ff = 2 (P <u>SE</u> 0.6372 0.8438 0.6784 ff = 2 (P	100.0% = 0.02); F <u>Weight</u> 40.8% 23.3% 36.0% 100.0%	1.15 [0.28, 4.68] ² = 74% Risk Ratio <u>IV, Random, 95% CI</u> 0.91 [0.26, 3.17] 1.36 [0.26, 7.10] 2.23 [0.59, 8.43] 1.38 [0.62, 3.06] ² = 0%		F IV. R: 	andom, 95°	% CI	
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Total (95% Cl) Heterogeneity: Tau ² = Test for overall effect: D Study or Subgroup Aminian 2019 Li W 2022 Saw 2017 Total (95% Cl) Heterogeneity: Tau ² = Test for overall effect: E Study or Subgroup	1.08; Chi ² = 7.63, c Z = 0.19 (P = 0.85) <u>log[Risk Ratio]</u> -0.0943 0.3067 0.802 0.00; Chi ² = 0.93, c Z = 0.79 (P = 0.43) <u>log[Risk Ratio]</u>	ff = 2 (P <u>SE</u> 0.6372 0.8438 0.6784 ff = 2 (P <u>SE</u>	100.0% = 0.02); F <u>Weight</u> 40.8% 23.3% 36.0% 100.0% = 0.63); F <u>Weight</u>	1.15 [0.28, 4.68] ² = 74% Risk Ratio <u>IV, Random, 95% CI</u> 0.91 [0.26, 3.17] 1.36 [0.26, 7.10] 2.23 [0.59, 8.43] 1.38 [0.62, 3.06] ² = 0% Risk Ratio <u>IV, Random, 95% CI</u>	0.01	F IV, R: 0.1	andom, 95°	<mark>% CI</mark> 10	
Total (95% Cl) Heterogeneity: Tau ² = Test for overall effect: D Study or Subgroup Aminian 2019 Li W 2022 Saw 2017 Total (95% Cl) Heterogeneity: Tau ² = Test for overall effect: E Study or Subgroup Aminian 2019	1.08; Chi ² = 7.63, c Z = 0.19 (P = 0.85) <u>log[Risk Ratio]</u> -0.0943 0.3067 0.802 0.00; Chi ² = 0.93, c Z = 0.79 (P = 0.43) <u>log[Risk Ratio]</u> 0.2624	ff = 2 (P <u>SE</u> 0.6372 0.8438 0.6784 ff = 2 (P <u>SE</u> 0.1505	100.0% = 0.02); F <u>Weight</u> 40.8% 23.3% 36.0% 100.0% = 0.63); F <u>Weight</u> 6.8%	1.15 [0.28, 4.68] ² = 74% Risk Ratio <u>IV, Random, 95% CI</u> 0.91 [0.26, 3.17] 1.36 [0.26, 7.10] 2.23 [0.59, 8.43] 1.38 [0.62, 3.06] ² = 0% Risk Ratio <u>IV, Random, 95% CI</u> 1.30 [0.97, 1.75]	0.01	F IV, R: 0.1	andom, 959	<mark>% CI</mark> 10	
Total (95% Cl) Heterogeneity: Tau ² = Test for overall effect: D Study or Subgroup Aminian 2019 Li W 2022 Saw 2017 Total (95% Cl) Heterogeneity: Tau ² = Test for overall effect: E Study or Subgroup	1.08; Chi ² = 7.63, c Z = 0.19 (P = 0.85) <u>log[Risk Ratio]</u> -0.0943 0.3067 0.802 0.00; Chi ² = 0.93, c Z = 0.79 (P = 0.43) <u>log[Risk Ratio]</u>	ff = 2 (P <u>SE</u> 0.6372 0.8438 0.6784 ff = 2 (P <u>SE</u> 0.1505	100.0% = 0.02); F <u>Weight</u> 40.8% 23.3% 36.0% 100.0% = 0.63); F <u>Weight</u> 6.8%	1.15 [0.28, 4.68] ² = 74% Risk Ratio <u>IV, Random, 95% CI</u> 0.91 [0.26, 3.17] 1.36 [0.26, 7.10] 2.23 [0.59, 8.43] 1.38 [0.62, 3.06] ² = 0% Risk Ratio <u>IV, Random, 95% CI</u>	0.01	F IV, R: 0.1	andom, 959	<mark>% CI</mark> 10	
Total (95% Cl) Heterogeneity: Tau ² = Test for overall effect: D Study or Subgroup Aminian 2019 Li W 2022 Saw 2017 Total (95% Cl) Heterogeneity: Tau ² = Test for overall effect: E Study or Subgroup Aminian 2019	1.08; Chi ² = 7.63, c Z = 0.19 (P = 0.85) <u>log[Risk Ratio]</u> -0.0943 0.3067 0.802 0.00; Chi ² = 0.93, c Z = 0.79 (P = 0.43) <u>log[Risk Ratio]</u> 0.2624	ff = 2 (P <u>SE</u> 0.6372 0.8438 0.6784 ff = 2 (P <u>SE</u> 0.1505 0.0415	100.0% = 0.02); F <u>Weight</u> 40.8% 23.3% 36.0% 100.0% = 0.63); F <u>Weight</u> 6.8% 89.3%	1.15 [0.28, 4.68] ² = 74% Risk Ratio <u>IV, Random, 95% CI</u> 0.91 [0.26, 3.17] 1.36 [0.26, 7.10] 2.23 [0.59, 8.43] 1.38 [0.62, 3.06] ² = 0% Risk Ratio <u>IV, Random, 95% CI</u> 1.30 [0.97, 1.75]	0.01	F IV, R: 0.1	andom, 959	<mark>% CI</mark> 10	
Total (95% Cl) Heterogeneity: Tau ² = Test for overall effect: D Study or Subgroup Aminian 2019 Li W 2022 Saw 2017 Total (95% Cl) Heterogeneity: Tau ² = Test for overall effect: E Study or Subgroup Aminian 2019 Dukkipati 2018	1.08; Chi ² = 7.63, c Z = 0.19 (P = 0.85) log[Risk Ratio] -0.0943 0.3067 0.802 0.00; Chi ² = 0.93, c Z = 0.79 (P = 0.43) log[Risk Ratio] 0.2624 0.2469	ff = 2 (P <u>SE</u> 0.6372 0.8438 0.6784 ff = 2 (P <u>SE</u> 0.1505 0.0415	100.0% = 0.02); F <u>Weight</u> 40.8% 23.3% 36.0% 100.0% = 0.63); F <u>Weight</u> 6.8% 89.3%	1.15 [0.28, 4.68] ² = 74% Risk Ratio <u>IV, Random, 95% CI</u> 0.91 [0.26, 3.17] 1.36 [0.26, 7.10] 2.23 [0.59, 8.43] 1.38 [0.62, 3.06] ² = 0% Risk Ratio <u>IV, Random, 95% CI</u> 1.30 [0.97, 1.75] 1.28 [1.18, 1.39]	0.01	F IV, R: 0.1	andom, 959	<mark>% CI</mark> 10	
Total (95% Cl) Heterogeneity: Tau ² = Test for overall effect: D Study or Subgroup Aminian 2019 Li W 2022 Saw 2017 Total (95% Cl) Heterogeneity: Tau ² = Test for overall effect: E Study or Subgroup Aminian 2019 Dukkipati 2018 Saw 2017	1.08; Chi ² = 7.63, c Z = 0.19 (P = 0.85) <u>log[Risk Ratio]</u> -0.0943 0.3067 0.802 0.00; Chi ² = 0.93, c Z = 0.79 (P = 0.43) <u>log[Risk Ratio]</u> 0.2624 0.2469 0.1133	ff = 2 (P <u>SE</u> 0.6372 0.8438 0.6784 ff = 2 (P <u>SE</u> 0.1505 0.0415 0.1978	100.0% = 0.02); F 40.8% 23.3% 36.0% 100.0% = 0.63); F <u>Weight</u> 6.8% 89.3% 3.9% 100.0%	1.15 [0.28, 4.68] ² = 74% Risk Ratio <u>IV, Random, 95% CI</u> 0.91 [0.26, 3.17] 1.36 [0.26, 7.10] 2.23 [0.59, 8.43] 1.38 [0.62, 3.06] ² = 0% Risk Ratio <u>IV, Random, 95% CI</u> 1.30 [0.97, 1.75] 1.28 [1.18, 1.39] 1.12 [0.76, 1.65] 1.27 [1.18, 1.38]	0.01	F IV, R: 0.1 F IV, R:	andom, 959	<mark>% CI</mark> 10	

10

Patients diagnosed with DRT may have persistent DRT or DRT recurrence after receiving anti-thrombotic therapies. Recent studies reported that only approximate a quarter of cases demonstrating persistent DRT presence in clinical follow-up (7, 45). And patients with persistent DRT showed higher stroke rates and increased mortality rates (45). And Asmarats et al. (46) firstly evaluated the recurrence of DRT, suggesting that thrombus recurrence was common, thus long-term OAC was encouraged after a first DRT. More specified anti-thrombotic regimens and more RCT are needed in prevention of DRT. Except for DRT, late DRT is thought to be less frequent because of device sealing, which remains variable on an individual basis. Furthermore, the collection of late DRT in this study is not comprehensive enough to carry out effective analysis. Consistent with our results, Sedaghat et al. (45) suggested that no clinical or echocardiographic predictors for late DRT formation could be identified in their study.

This meta-analysis has several limitations. First, because of limited randomized data, this meta-analysis included both randomized and observational studies. The observational studies are subjected to unmeasured confounding and selection bias. Therefore, consistent with previous meta-analysis of DRT (47), we conducted sensitivity analysis by including MCR and RCT only to test the inconsistency, which could verify the feasibility of the inclusion of multiple studies. Second, the definition of some clinical events such as major procedurerelated complications was not unanimous across studies; however, it was less likely to have a huge impact on our final conclusion. Third, the follow-up duration in each study varied, which may have negative influence on outcomes. Last but not least, due to the paucity of individual data in each eligible study, no subgroup analysis was done according to different generations of SS and DS.

Conclusion

Device related thrombus is an infrequent complication of LAAC, associated with increased rates of ischemic events. The incidence of DRT was comparable between SS and DS devices. The occurrence rate of stroke and SE associated DRT was similar in devices with different occlusion mechanisms. Further large multicenter prospective studies are needed to confirm the true prevalence of DRT and to evaluate the risk factors, associated complications and treatment regimens.

Data availability statement

The original contributions presented in this study are included in the article/Supplementary material, further inquiries can be directed to the corresponding author.

Author contributions

SZ: data curation (lead), formal analysis (equal), investigation (equal), methodology (equal), software (lead), validation (equal), visualization (equal), writing - original draft (equal), and writing - review and editing (equal). S-HX: data curation (equal), formal analysis (equal), investigation (equal), methodology (equal), validation (equal), visualization (equal), writing - original draft (equal), and writing - review and editing (equal). Y-GG: methodology (equal), software (lead), and writing - review and editing (equal). X-XZ and Z-FG: supervision (equal), investigation (equal), methodology (equal), and writing - review and editing (equal). Y-WQ: supervision (equal), investigation (equal), and writing - review and editing (equal). YB: conceptualization (lead), resources (lead), writing - original draft (equal), writing - review and editing (equal), supervision (lead), and taken responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation. All authors contributed to the article and approved the submitted version.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Supplementary material

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/ fcvm.2022.1088782/full#supplementary-material

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