Metanalisi di confronto tra terapia antiaggregante e anticoagulanti orali diretti dopo chiusura percutanea dell'auricola sinistra

Background

- Percutaneous left atrial appendage closure (LAAC) is currently an alternative treatment in patients with non-valvular atrial fibrillation who are not candidates for long-term oral anticoagulation.
- The typical devices used are either a Watchman (Boston Scientific, Marlborough, MA), Amplatzer Cardiac Plug (St. Jude Medical, Minneapolis, MN), or Amplatzer Amulet (St. Jude Medical, Minneapolis, MN).
- The rate of device-related thrombus (DRT) has a reported onset of 30 to 90 days after the procedure.
- Therefore, medical management is warranted to decrease this risk

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Table 18 (part 1). Antithrombotic therapy before and after LAAO

Clinical situation and therapeutic concept	Consensus statement	Symbol	References
Acetylsalicylic acid 75-325 mg/day for the procedure and then continued long term (load 300-500 mg prior to procedure if not previously on acetylsalicylic acid)	"Should do this"		108,114,140,173
Anticoagulation, using unfractionated heparin, is recommended during the implantation procedure prior to or immediately after TSP, aiming for an activated clotting time of >250 s	"Should do this"		106,165
After WATCHMAN implantation, warfarin (INR 2-3) should be given for 45 days, followed by clopidogrel for 6 months after the procedure in low bleeding risk group of patients, while in high bleeding risk group OAC should not be applied	"Should do this"		106,108
NOAC is a possible alternative to warfarin after WATCHMAN implantation	"May do this"		157,166–168
After WATCHMAN implantation in patients not suitable for oral anticoagulation, DAPT including clopidogrel 75 mg/day for 1 to 6 months after the procedure (load 300-600 mg prior to procedure if not previously on clopidogrel)	"May do this"		106,108,174
After AMPLATZER Cardiac Plug or Amulet implantation, DAPT including clopidogrel 75 mg/ day for 1 to 6 months after the procedure (load 300-600 mg prior to procedure if not previously on clopidogrel)	"May do this"		115,173
Other options that may be considered on a case-by-case basis include a single antiplatelet therapy (acetylsalicylic acid or clopidogrel) for short periods of time, as long as approved by a team consensus	"May do this"		175

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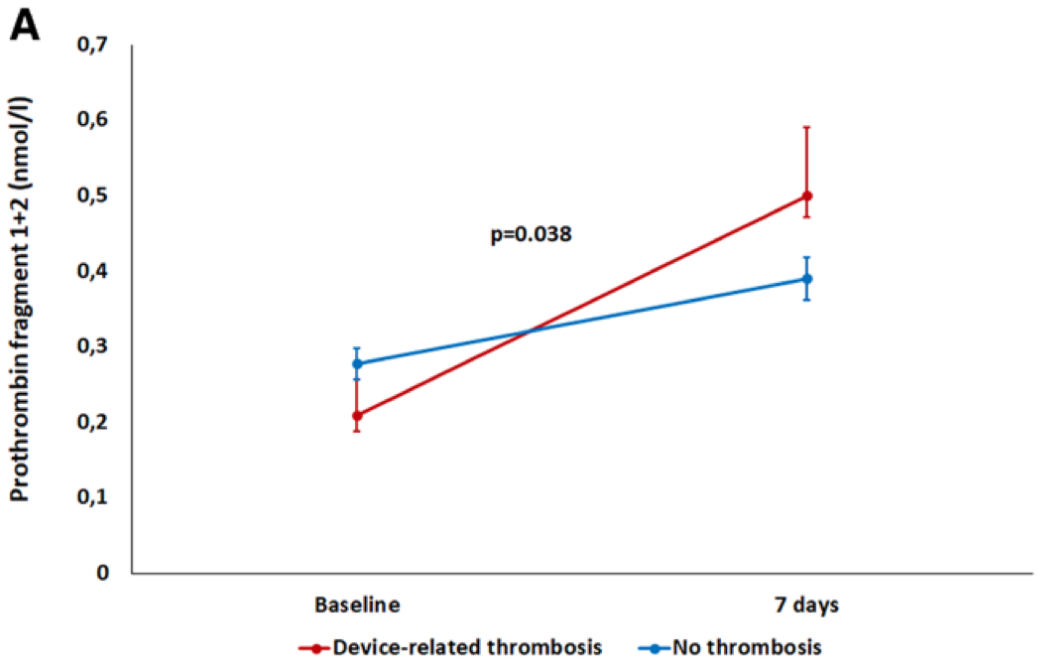
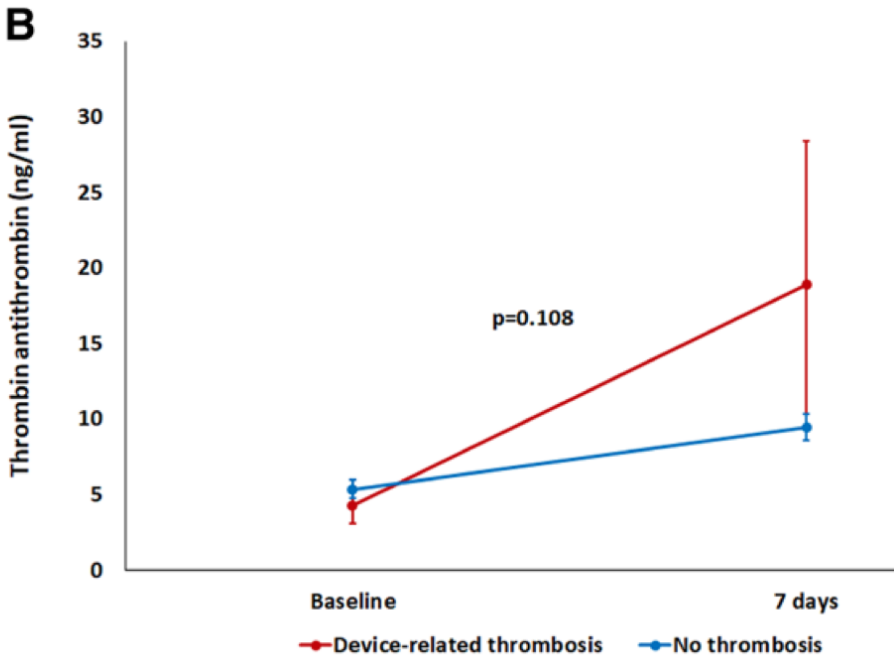
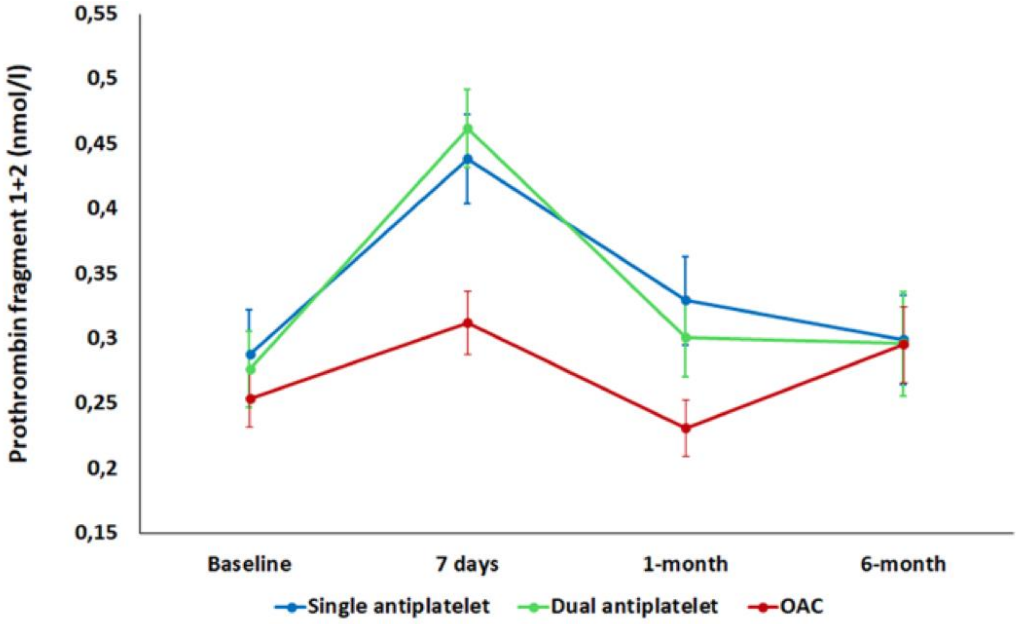
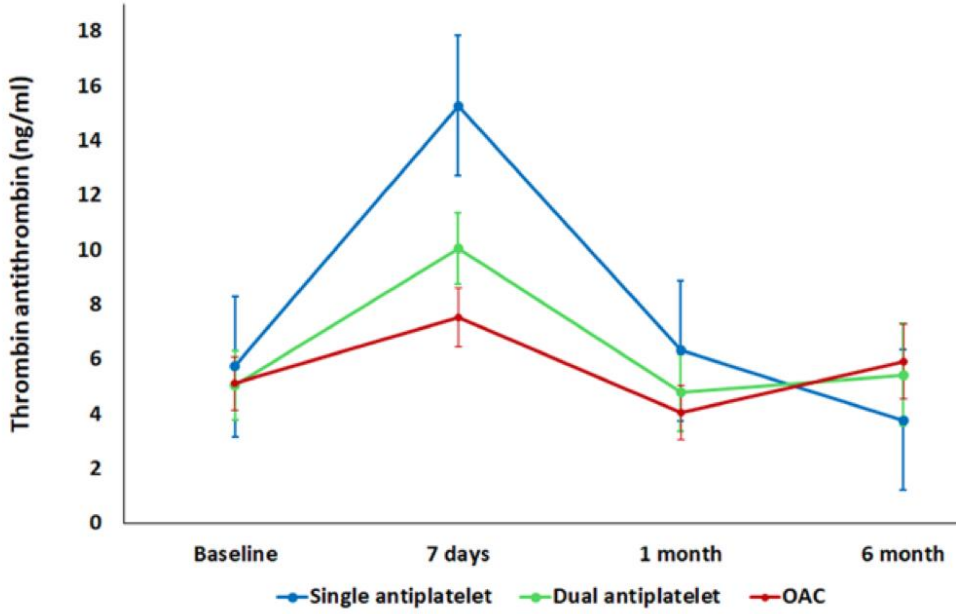
Coagulation system activation post LAAC









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Meta-Analysis Comparing Antiplatelet Therapy Versus Direct Oral Anticoagulation in Percutaneous Left Atrial Appendage Closure

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Methods

- The PubMed, EMBASE, and COCHRANE databases were searched for relevant articles published from inception to May 2, 2021.
- Included all randomized controlled studies that compared APT vs DOACs in patients with LAAC.
- The primary outcome was stroke and the secondary outcomes were major bleeding, DRT, and all-cause mortality.
- Fifteen RCTs were included with a total of 1,946 patients.

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Results

- The rate of stroke was numerically lower in the DOACs arm when compared to the APT arm, but this difference did not reach statistical significance (APT 2.2% vs DOAC 1.0%, $p = 0.26$).
- Major bleeding: APT 5.27% vs DOAC 3.53%, $p = 0.16$.
- DRT: APT 6.32% vs DOAC 2.5%, $p = 0.65$.
- All-cause mortality: 12.97% vs 6.33%, $p = 0.23$.
- Sensitivity analysis showed that heterogeneity across the trials was low-moderate ($I^2 = 0\%$ to 53%).

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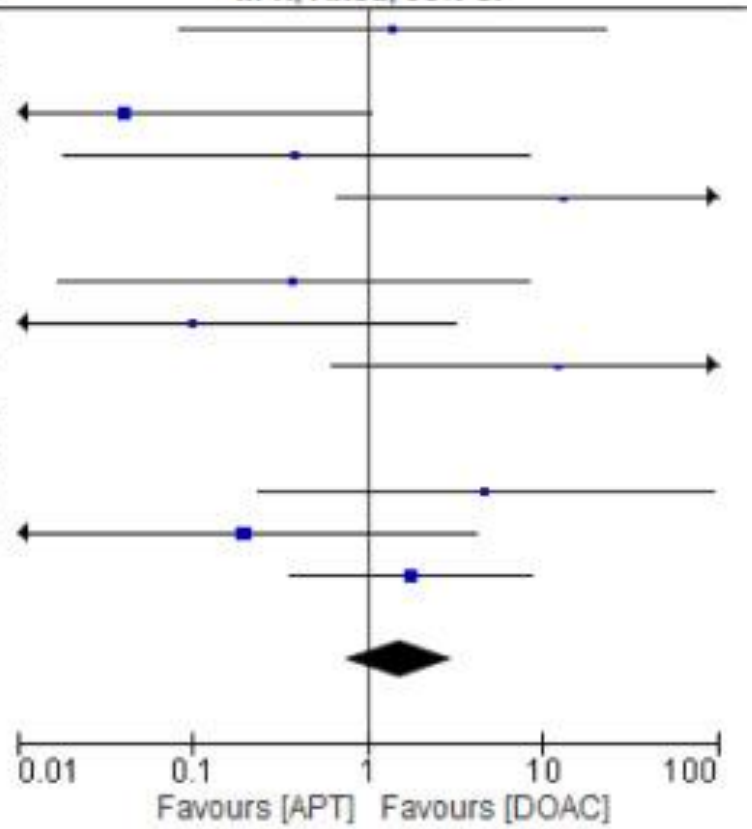
Stroke

A. Stroke

Study or Subgroup	APT Events	APT Total	DOAC Events	DOAC Total	Weight	Odds Ratio M-H, Fixed, 95% CI	Year
Wiebe 2015	1	41	1	57	6.5%	1.40 [0.09, 23.05]	2015
Bosche 2015	0	27	0	18		Not estimable	2015
Wolfrum 2016	0	150	1	19	21.0%	0.04 [0.00, 1.04]	2016
Budts 2016	3	119	0	6	7.3%	0.39 [0.02, 8.39]	2016
Kim 2016	3	35	0	61	2.6%	13.25 [0.66, 264.34]	2016
Seidel 2017	0	50	0	62		Not estimable	2017
Nielsen-Kudsk 2017	2	141	0	10	7.2%	0.38 [0.02, 8.36]	2017
Jalal 2017	1	74	0	2	7.5%	0.10 [0.00, 3.18]	2017
Lim 2017	5	19	0	16	3.1%	12.52 [0.64, 246.38]	2017
Tarantini 2018	0	12	0	11		Not estimable	2018
Yazdani 2018	0	70	0	17		Not estimable	2018
Asmarats 2020	3	48	0	30	4.5%	4.69 [0.23, 94.10]	2020
Liu 2020	0	174	2	174	19.8%	0.20 [0.01, 4.15]	2020
Faroux 2021	7	190	2	95	20.4%	1.78 [0.36, 8.73]	2021
Total (95% CI)		**1150**		**578**	**100.0%**	**1.52 [0.73, 3.13]**	
Total events	25		6				

Heterogeneity: Chi² = 14.92, df = 9 (P = 0.09); I² = 40%

Test for overall effect: Z = 1.12 (P = 0.26)



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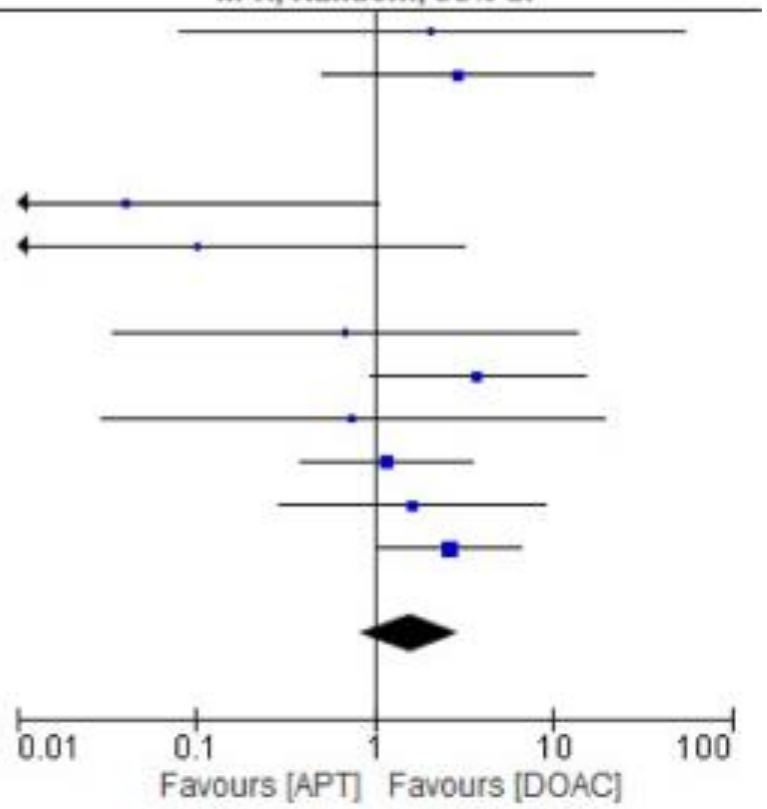
Major bleeding

B. Major Bleeding

Study or Subgroup	APT Events	APT Total	DOAC Events	DOAC Total	Weight	Odds Ratio M-H, Random, 95% CI	Year
Bosche 2015	1	27	0	18	3.6%	2.09 [0.08, 54.30]	2015
Wiebe 2015	4	41	2	57	10.6%	2.97 [0.52, 17.07]	2015
Budts 2016	0	119	0	6		Not estimable	2016
Kim 2016	0	35	0	61		Not estimable	2016
Wolfrum 2016	0	150	1	19	3.6%	0.04 [0.00, 1.04]	2016
Jalal 2017	1	74	0	2	3.2%	0.10 [0.00, 3.18]	2017
Lim 2017	0	19	0	16		Not estimable	2017
Nielsen-Kudsk 2017	4	141	0	10	4.2%	0.69 [0.03, 13.64]	2017
Seidel 2017	8	50	3	62	15.0%	3.75 [0.94, 14.96]	2017
Yazdani 2018	1	70	0	17	3.6%	0.76 [0.03, 19.35]	2018
Liu 2020	7	174	6	174	20.2%	1.17 [0.39, 3.57]	2020
Asmarats 2020	5	48	2	30	11.0%	1.63 [0.30, 8.98]	2020
Faroux 2021	29	190	6	95	25.1%	2.67 [1.07, 6.68]	2021
Total (95% CI)		**1138**		**567**	**100.0%**	**1.58 [0.84, 2.99]**	
Total events	60		20				

Heterogeneity: Tau² = 0.20; Chi² = 11.30, df = 9 (P = 0.26); I² = 20%

Test for overall effect: Z = 1.41 (P = 0.16)



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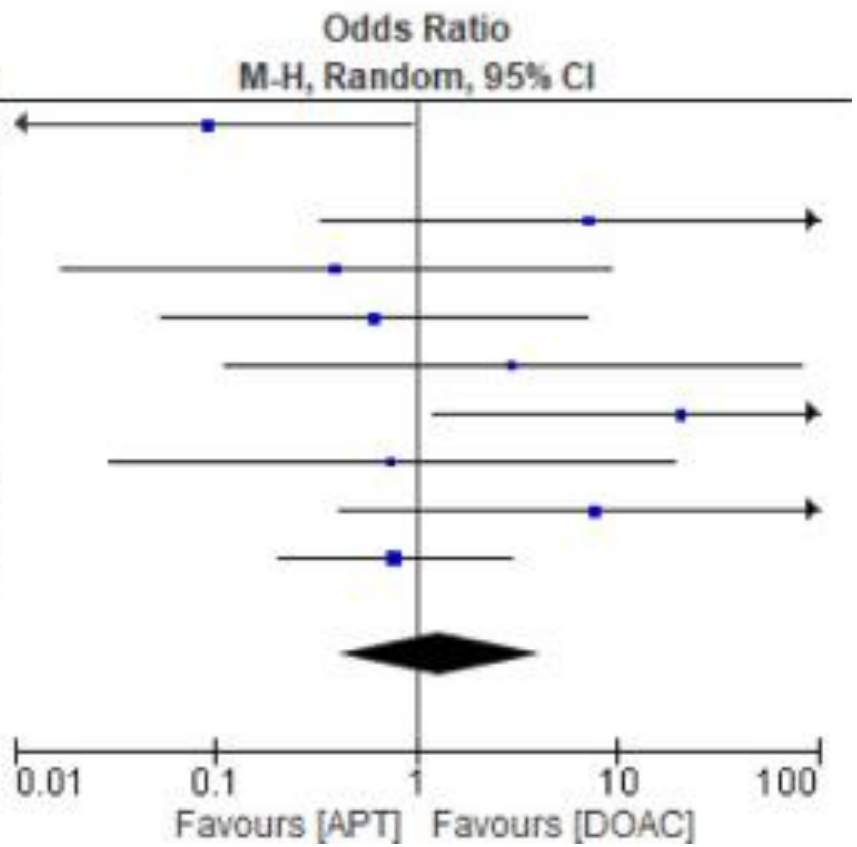
Device-related thrombus

C. Device-related thrombus

Study or Subgroup	APT Events	APT Total	DOAC Events	DOAC Total	Weight	Odds Ratio M-H, Random, 95% CI	Year
Chun 2013	1	59	3	19	12.8%	0.09 [0.01, 0.94]	2013
Bosche 2015	0	27	0	18		Not estimable	2015
Wiebe 2015	2	41	0	57	9.3%	7.28 [0.34, 155.74]	2015
Jalal 2017	5	74	0	2	8.9%	0.40 [0.02, 9.31]	2017
Seidel 2017	1	50	2	62	12.2%	0.61 [0.05, 6.95]	2017
Tarantini 2018	1	12	0	11	8.4%	3.00 [0.11, 81.61]	2018
Cochet 2018	19	83	0	34	10.2%	20.86 [1.22, 356.11]	2018
Yazdani 2018	1	70	0	17	8.6%	0.76 [0.03, 19.35]	2018
Asmarats 2020	5	48	0	30	9.8%	7.71 [0.41, 144.70]	2020
Liu 2020	4	153	5	150	19.7%	0.78 [0.20, 2.96]	2020
Total (95% CI)		**617**		**400**	**100.0%**	**1.30 [0.41, 4.14]**	
Total events	39		10				

Heterogeneity: Tau² = 1.30; Chi² = 14.28, df = 8 (P = 0.07); I² = 44%

Test for overall effect: Z = 0.45 (P = 0.65)



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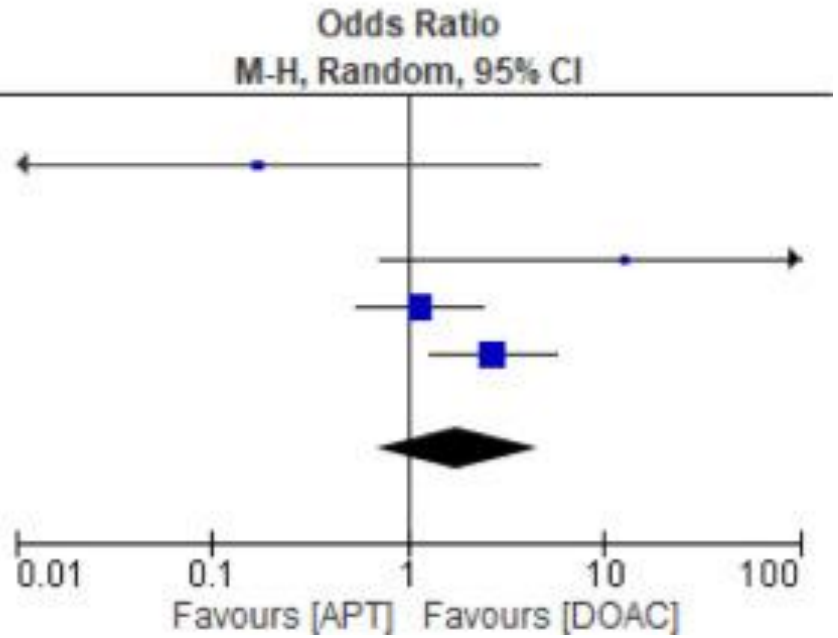
All-cause mortality

D. All-cause mortality

Study or Subgroup	APT Events	APT Total	DOAC Events	DOAC Total	Weight	Odds Ratio M-H, Random, 95% CI	Year
Seidel 2017	0	50	0	62		Not estimable	2017
Jalal 2017	2	74	0	2	7.3%	0.17 [0.01, 4.62]	2017
Lim 2017	0	19	0	16		Not estimable	2017
Asmarats 2020	8	48	0	30	9.1%	12.80 [0.71, 230.50]	2020
Liu 2020	16	174	14	174	41.6%	1.16 [0.55, 2.45]	2020
Faroux 2021	46	190	10	95	42.0%	2.72 [1.30, 5.66]	2021
Total (95% CI)		**555**		**379**	**100.0%**	**1.79 [0.69, 4.65]**	
Total events	72		24				

Heterogeneity: $Tau^2 = 0.42$; $Chi^2 = 6.45$, $df = 3$ ($P = 0.09$); $I^2 = 53\%$

Test for overall effect: $Z = 1.20$ ($P = 0.23$)



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Limitation

- APT arm included patients on single and dual APT, thus the efficacy and safety of single versus dual APT is unclear.
- Comparison should be done between the three different types of LAAC devices, which includes Watchman, Amplatzer Cardiac Plug, or Amplatzer Amulet.

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Conclusions

- DOACs have numerically lower rates of stroke, major bleeding, DRT, and all-cause mortality when compared to APT, but the difference did not reach statistical significance.

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