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ORIGINAL ARTICLE

Patent Foramen Ovale Closure Versus Medical Therapy for Cryptogenic Stroke: Meta-Analysis of Randomised Trials

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Background Patent foramen ovale (PFO) is a common anatomic variant associated with cryptogenic stroke. Percutaneous PFO closure in these patients to prevent recurrent neurological events has been controversial for decades, and mixed results have been reported from past and recent observational and randomised studies. This meta-analysis of randomised trials aims to compare the efficacy and safety of PFO closure with medical therapy for cryptogenic stroke patients.

Methods Medline, PubMed, EMBASE, Scopus and Cochrane were searched from January 1980 to September 2017 by two authors independently to include original randomised trials comparing PFO closure with medical therapy for secondary stroke prevention. Relevant study and baseline characteristics and outcomes were extracted and pooled using random-effects models.

Results Amongst 619 articles searched giving 10 full-texts assessed, six studies reporting five randomised trials and totalling 1,829 PFO closure and 1,611 medical therapy patients were included. Pooled hazards ratios (95% confidence interval, p-value) ischaemic stroke, transient ischaemic attack (TIA) and composite neurovascular or mortality events were 0.41 (0.19–0.90, $p = 0.03$), 0.77 (0.51–1.14, $p = 0.19$) and 0.60 (0.44–0.81, $p < 0.001$) for PFO closure compared to medical therapy. Any adverse events, major bleeding and all-cause mortality were similar between modalities ($p = 0.37$–0.95), however PFO closure had higher rates of new onset atrial fibrillation at 4.6 times ($p < 0.001$).

Conclusion Our meta-analysis found that, in patients with cryptogenic stroke, percutaneous PFO closure is beneficial at reducing ischaemic stroke and composite neurovascular or mortality events, with a higher incidence of new atrial fibrillation, compared to medical therapy.

Keywords Patent foramen ovale • Stroke

Introduction

Cryptogenic strokes make up 25–35% of all strokes [1,2]. Patent foramen ovale (PFO) is a common anatomical variant present in about 25% of the general population, and is significantly associated with cryptogenic strokes across all age groups [2–4]. These patients, managed with medical therapy alone, continue to have recurrent stroke rates higher than the general population [5], making PFO closure, if effective, an attractive option. Observational studies looked promising for intervention [6,7], however earlier randomised trials were negative for their primary efficacy endpoints [8–10]. Two (2)

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further randomised studies were recently presented and published in 2017 with favourable outcomes [11,12]. This meta-analysis sought to pool the findings of existing randomised trials to compare the efficacy of stroke prevention between PFO closure and medical therapy.

Methods

The meta-analysis was conducted in accordance with the PRISMA guidelines. The literature search was performed using five electronic databases (Cochrane Central, EMBASE, Medline, PubMed, and Scopus) to identify potentially relevant articles and abstracts published between 1 January 1980 and 17 September 2017. Search terms and corresponding MeSH and Emtree terms used in combination included, ''patent foramen ovale'', ''PFO'', ''atrial septal aneurysm'', ''interatrial shunt''; ''stroke'', ''cerebrovascular accident'', ''CVA'', ''transient ischaemic attack'', ''TIA'', ''cerebral infarction''; and ''percutaneous closure'', ''transcatheter closure'', ''cardiac catheterization'', and ''septal occluder device''. The reference lists of searched and review articles were also screened for potentially relevant articles and conference abstracts. Two (2) investigators (TKMW and MTMW) independently conducted the literature search and evaluated studies for inclusion, with discrepancies resolved by consensus.

Randomised controlled trials comparing the efficacy of patent foramen ovale closure and antiplatelet and/or anticoagulation medical therapy in preventing recurrent vascular events (stroke and transient ischaemic attack) and mortality in adult human patients (over 18 years of age) were eligible for inclusion. When multiple publications reported results from the same trial, they were reviewed as a single study.

Two investigators (TW and MW) independently extracted data on study design, baseline patient characteristics, study outcomes and adverse events, using standardised forms. Both the published article and appendices were reviewed. Differences between investigators were then resolved by consensus.

Statistical meta-analysis was performed using Review Manager version 5.3 (Cochrane Collaboration, UK) to calculate pooled intention to treat odds ratios. Random effect modelling was used to account for potential variation in methodology and participant characteristics between studies. All tests were two-tailed and $p < 0.05$ considered significant.

Results

The study selection process is illustrated in Figure 1. The initial literature search identified 619 articles. Following

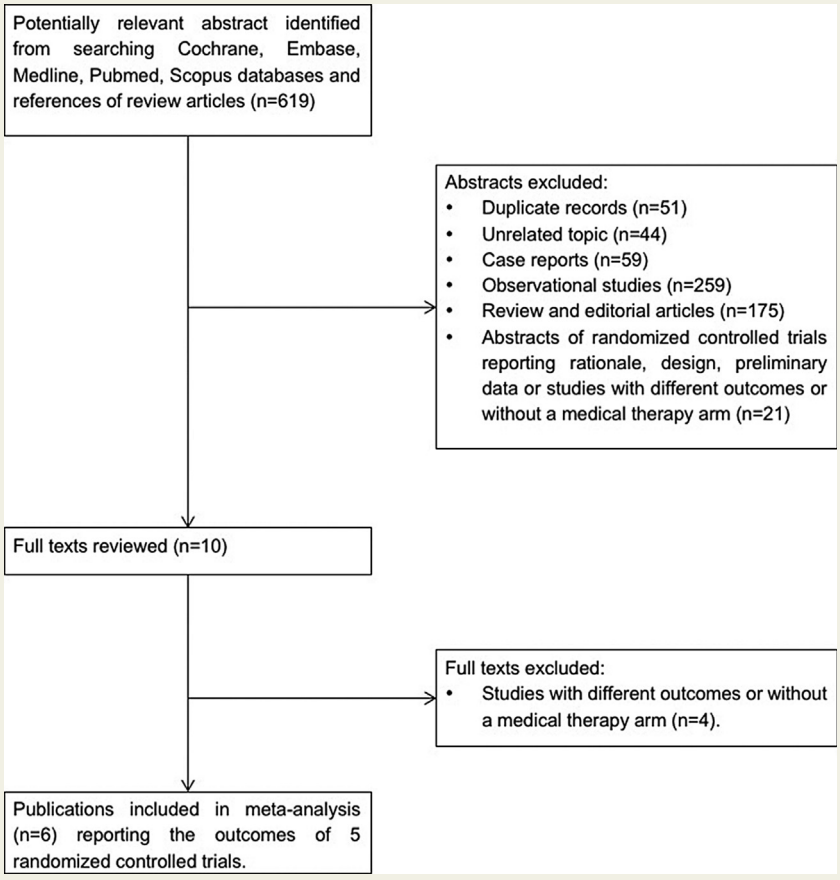

Figure 1 Flow diagram of study selection.

abstract and full text review and exclusion, six publications reporting five randomised controlled trials were included [7–12]. There were good levels of inter-observer agreement for study inclusion (kappa = 1.0) and data abstraction (kappa = 0.93).

Tables 1 and 2 describe the study design and baseline patient characteristics of the five randomised trials. A total of 3,440 patients were enrolled, of which 1,829 were randomised to patent foramen ovale closure, and 1,611 to medical therapy, with mean age of 45 years and 55% being male.

Study outcome rates are described in Table 3, with pooled forest plots of efficacy and safety endpoints in Figure 2 and 3 respectively. Patients randomised to PFO closure had a significantly lower occurrence of both stroke (2.0% versus 4.5%, OR 0.41, 95% CI: 0.19–0.90, p = 0.03, I^2 = 59%,), and the composite outcome of neurovascular events and mortality (4.3% versus 6.8%, OR 0.60, 95% CI: 0.44–0.81, p = 0.0009, I^2 = 0%) than those on medical therapy. Although transient ischaemic attacks occurred in a lower proportion of patients treated with PFO closure, the inter-group difference was not statistically significant (2.4% versus 3.5%, OR 0.77, 95% CI:0.51–1.14, p = 0.19, I^2 = 0%).

In terms of adverse events, no significant differences were observed in overall occurrence of any adverse events, major bleeding, or all cause mortality (all $p > 0.05$). The exception is new onset atrial fibrillation, which was more common among patients in the PFO closure group (4.1% versus 0.7%, OR 4.62, 95% CI: 2.03–10.49, p = 0.0003, I^2 = 35%). All studies reported that atrial fibrillations occurring in the PFO closure were in the majority either transient and/or occurred within the admission or 30 days at 60–90% with rare associated complications (one stroke reported in one trial with 29 having atrial fibrillation [11]).

Subgroup analysis of primary outcomes displayed in Table 4 showed that significant reductions in primary study outcomes of neurovascular events were limited to men and those aged less than 45 years (both $p < 0.05$).

Discussion

The optimal management strategy for patients with cryptogenic stroke and patent foramen ovale has long been controversial. Guidelines do not make recommendations regarding lifestyle interventions, statins or antihypertensives [14]. Multiple observational studies and a randomised trial have not found statistically significant differences in the efficacy of anticoagulants compared to antiplatelet therapy [15,16], so the former is only recommended in patients with concurrent venous thromboembolism, and if contraindicated, inferior vena cava filter insertion is an alternative [14]. There remains an unmet need due to recurrence of neurological events in these patients on medical therapy, which is why PFO closure gained significant interest and traction to be undertaken and studied, for the last 2 decades [5,17].

The long-awaited randomised evidence initially came out one after the other in three trials during 2012–2013 [8–10]. All three trials, however, found no statistical difference in their intention-to-treat analysis of primary efficacy endpoints of composite stroke, mortality with or without TIA and other embolism, or indeed endpoints in isolation, compared to medical therapy. To try and improve power, many meta-analyses pooling data from the same three studies were performed and published, however these blurred the interpretation more with some concluding PFO closure to be beneficial [18,19], while others found no difference [20–22]. As efficacy remained unproven, with individual trials all negative and meta-analyses results being mixed, subsequent clinical practice and guidelines did not recommend percutaneous PFO closure in these patients [14].

Three more studies of two new trials and extended follow-up of the original Randomized Evaluation of Recurrent Stroke Comparing PFO Closure to Established Current Standard of Care Treatment (RESPECT) trial were recently published [11–13]. In contrast to the earlier trials, all three trials were positive for primary efficacy endpoints and some of the individual endpoints. There were some important differences which may have influenced the outcomes. Apart from RESPECT, the newer trials had approximately double the number of participants than the older trials and therefore increased power [8–13]. The control group for the two latest trials were antiplatelet therapy, but that of the three earlier ones were antiplatelet and/or anticoagulants which may have had albeit small differences in their outcome rates [11,12]. The newer trials did not have patients with transient ischaemic attack, and the endpoints were purely stroke and didn't include mortality, which is not the purpose of PFO closure. Furthermore, the newer trials were also a more selective group of cryptogenic stroke patients with PFO, perhaps what the investigators hypothesised where there would be of greater benefit, with right-to-left shunting PFO and neuroimaging performed in GORE® HELEX® Septal Occluder / GORE® CARDIOFORM Septal Occluder for Patent Foramen Ovale (PFO) Closure in Stroke Patients (Gore-REDUCE) [11], and presence of atrial septal aneurysm or large interatrial-shunt in Patent Foramen Ovale Closure or Anticoagulants versus Antiplatelet Therapy to Prevent Stroke Recurrence (CLOSE) [12], which may somewhat influence the generalisability of the positive findings.

Pooling data of all the trials showed that stroke rates and composite neurovascular events and mortality rates significantly favoured PFO closure. Although having statistical significance (both $p < 0.05$), and promising odds ratios of 0.41 and 0.60 respectively for these endpoints, pooled absolute risk difference was 2.5% for both, giving a modest number needed to treat of 40 [8–13]. Part of the reason for this is the low event rates such as 4.5% stroke over the mean follow-up period which may be a result of low prevalence of vascular risk factors and younger age. Despite this there is also some evidence that, although procedural cost is high, the reduced event rates and less long-term medications may offset this to make PFO closure cost effective in the long term, but further studies are required [23]. As a result of this

Table 1 Study design of randomised controlled trials.

Trial	Authors	Year	Enrolment period	Enrolment institution	Treatment		No. of patients		Median follow-up (months)	Lost to follow-up, no. (%)	
					PFO closure	Medical therapy	PFO closure	Medical therapy		PFO closure	Medical therapy
CLOSE [12]	Mas	2017	2007-2016	Multicentre (34 centres in France and Germany)	PFO closure[1] + aspirin and clopidogrel (3 months) + aspirin, clopidogrel, or aspirin and dipyridamole.	Aspirin, clopidogrel, or aspirin and dipyridamole.	238	235	64	0 (0.0%)	2 (0.9%)
CLOSURE I [8]	Furlan	2012	2003-2008	Multicentre (87 centres in United States and Canada)	Starflex septal occluder + aspirin (2 years) + clopidogrel (6 months)	Aspirin, coumadin, or aspirin and coumadin.	447	462	44	24 (5.4%)	77 (6.7%)
Gore REDUCE [11]	Søndergaard	2017	2008-2015	Multicentre (63 centres in Canada, Denmark, Finland, Norway, Sweden, United Kingdom and United States)	Helex septal occluder or cardioform septal Occluder + clopidogrel (3 days) + aspirin, aspirin and dipyridamole, or clopidogrel	Aspirin, aspirin and dipyridamole, or clopidogrel	441	223	38	16 (3.6%)	7 (3.1%)
PC Trial [9]	Meier	2013	2000-2009	Multicentre (29 centres in Europe, Canada, Brazil, and Australia)	Amplatzer PFO occluder + aspirin (5-6 months) + ticlopidine or clopidogrel	Antiplatelet, or antiplatelet and coumadin.	204	210	49	24 (11.8%)	31 (14.8%)
RESPECT [10,13]	Carroll	2013	2003-2011	Multicentre (69 centres in United States and Canada)	Amplatzer PFO occluder + aspirin and clopidogrel (1 month) + aspirin (at least 5 months)	Aspirin, coumadin, clopidogrel, aspirin and dipyridamole, or aspirin and clopidogrel.	499	481	31	19 (3.8%)	27 (5.6%)
	Saver	2017							71	60 (12.0%)	67 (13.9%)
Total							1829	1611	47	124 (6.8%)	184 (11.4%)

Abbreviations: CLOSE, Patent Foramen Ovale Closure or Anticoagulants versus Antiplatelet Therapy to Prevent Stroke Recurrence; Gore REDUCE, GORE® HELEX® Septal Occluder / GORE® CARDIOFORM Septal Occluder for Patent Foramen Ovale (PFO) Closure in Stroke Patients; RESPECT, Randomized Evaluation of Recurrent Stroke Comparing PFO Closure to Established Current Standard of Care Treatment.

[1]PFO closure was conducted with one of the following devices: Amplatzer PFO occluder, Intrasept PFO occluder, Premere, Starflex septal occluder, Amplatzer cribriform occluder, Figulla Flex II PFO occluder, Atriasept II ocluder, Amplatzer ASD occluder, Figulla Flex II UNI occluder, Gore septal occluder, or Figulla Flex II ASD occluder.

Table 2 Baseline characteristics of randomised controlled trials.

Trial	Treatment Group	Age (years), mean ± SD	Male gender, no. (%)	Atrial septal aneurysm, no. (%)	Hypertension, no. (%)	Hyperlipidaemia, no. (%)	Smoking, no. (%)	Diabetes, no. (%)
CLOSE	PFO closure	42.9 ± 10.1	137 (57.6%)	81 (34.0%)	27 (11.3%)	30 (12.6%)	68 (28.6%)	3 (1.3%)
	Medical therapy	43.8 ± 10.5	142 (60.4%)	74 (31.5%)	24 (10.2%)	36 (15.3%)	69 (29.4%)	9 (3.8%)
CLOSURE I	PFO closure	46.3 ± 9.6	233 (52.1%)	168 (37.6%)	151 (33.8%)	212 (47.4%)	96 (21.5%)	N/R
	Medical therapy	45.7 ± 9.1	238 (51.5%)	165 (35.7%)	131 (28.4%)	189 (40.9%)	104 (22.5%)	N/R
Gore REDUCE	PFO closure	45.4 ± 9.3	261 (59.2%)	86 (19.5%)	112 (25.4%)	N/R	63 (14.3%)	18 (4.1%)
	Medical therapy	44.8 ± 9.6	138 (61.9%)	N/R	58 (26.0%)	N/R	25 (11.2%)	10 (4.5%)
PC Trial	PFO closure	44.3 ± 10.2	92 (45.1%)	47 (23.0%)	49 (24.0%)	50 (24.5%)	52 (25.5%)	5 (2.5%)
	Medical therapy	44.6 ± 10.1	114 (54.3%)	51 (24.3%)	58 (27.6%)	62 (29.5%)	47 (22.4%)	6 (2.9%)
RESPECT	PFO closure	45.7 ± 9.7	268 (53.7%)	180 (36.1%)	158 (31.7%)	194 (38.9%)	75 (15.0%)	33 (6.6%)
	Medical therapy	46.2 ± 10.0	268 (55.7%)	169 (35.1%)	150 (31.2%)	193 (40.1%)	55 (11.4%)	40 (8.3%)
Total	PFO closure	45.3 ± 9.7	991 (54.2%)	562 (30.7%)	497 (27.2%)	486 (35.0%)	354 (19.4%)	59 (4.3%)
	Medical therapy	45.3 ± 9.8	900 (55.9%)	459 (33.1%)	421 (26.1%)	480 (34.6%)	300 (18.6%)	65 (5.7%)

Abbreviations: CLOSE, Patent Foramen Ovale Closure or Anticoagulants versus Antiplatelet Therapy to Prevent Stroke Recurrence; Gore REDUCE, GORE® HELEX® Septal Occluder / GORE® CARDIOFORM Septal Occluder for Patent Foramen Ovale (PFO) Closure in Stroke Patients; RESPECT, Randomized Evaluation of Recurrent Stroke Comparing PFO Closure to Established Current Standard of Care Treatment.

Table 3 Study outcomes of randomised controlled trials.

Trial	Treatment Group	Stroke, no. (%)	Transient ischaemic attack, no. (%)	Composite outcome of neurovascular events and mortality, no. (%)	Any adverse event, no. (%)	Procedural complications, no. (%)
CLOSE	PFO closure	0 (0.0%)	8 (3.4%)	8 (3.4%)	85 (35.7%)	14 (5.9%)
	Medical therapy	14 (6.0%)	8 (3.4%)	21 (8.9%)	78 (33.2%)	
CLOSURE I	PFO closure	12 (2.7%)	13 (2.9%)	23 (5.1%)	68 (15.2%)	13 (2.9%)
	Medical therapy	13 (2.8%)	17 (3.7%)	29 (6.3%)	76 (16.5%)	
Gore REDUCE	PFO closure	6 (1.4%)	1 (0.2%)	22 (5.0%)	62 (27.8%)	3 (1.5%)
	Medical therapy	12 (5.4%)	1 (0.4%)	20 (9.0%)	71 (34.8%)	
PC Trial	PFO closure	1 (0.5%)	5 (2.5%)	7 (3.4%)	62 (29.5%)	3 (0.6%)
	Medical therapy	5 (2.4%)	7 (3.3%)	11 (5.2%)	201 (40.3%)	
RESPECT	PFO closure	18 (3.6%)	17 (3.4%)	18 (3.6%)	173 (36.0%)	11 (2.5%)
	Medical therapy	28 (5.8%)	23 (4.8%)	28 (5.8%)	102 (23.1%)	
Total	PFO closure	37 (2.0%)	44 (2.4%)	78 (4.3%)	527 (28.8%)	44 (2.4%)
	Medical therapy	72 (4.5%)	56 (3.5%)	109 (6.8%)	451 (28.0%)	
	Odds ratio (95% CI)	0.41 (0.19-0.90)	0.77 (0.51-1.14)	0.60 (0.44-0.81)	1.05 (0.88-1.25)	
	p-value	0.03	0.19	0.0009	0.58	

Abbreviations: CLOSE, Patent Foramen Ovale Closure or Anticoagulants versus Antiplatelet Therapy to Prevent Stroke Recurrence; Gore REDUCE, GORE® HELEX® Septal Occluder / GORE® CARDIOFORM Septal Occluder for Patent Foramen Ovale (PFO) Closure in Stroke Patients; RESPECT, Randomized Evaluation of Recurrent Stroke Comparing PFO Closure to Established Current Standard of Care Treatment.

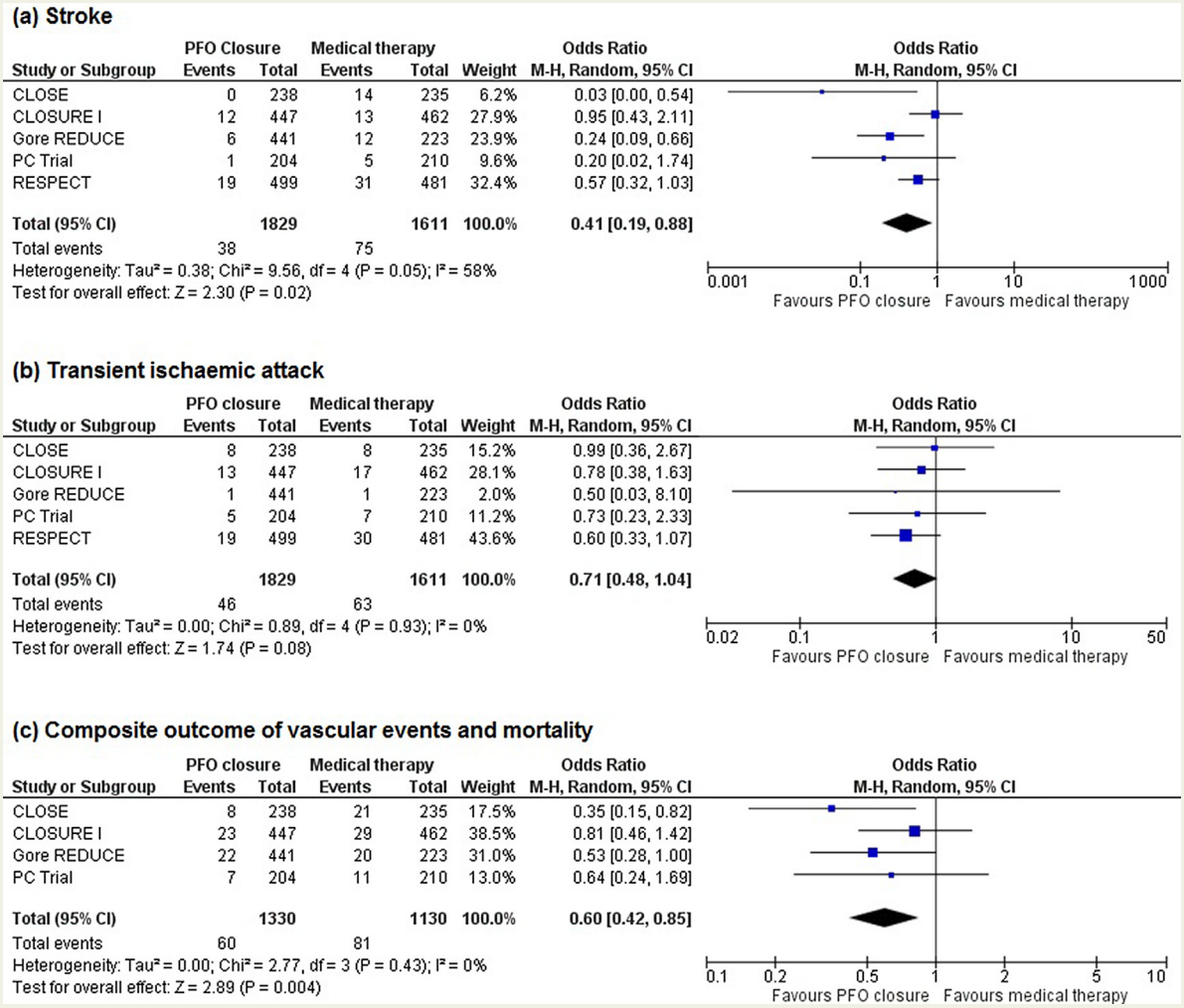

Figure 2 Efficacy Forest plots of odds ratio of (a) stroke, (b) transient ischaemic attack, and (c) composite neurovascular or mortality events, in patients randomised to patent foramen ovale (PFO) closure and medical therapy.

analysis, PFO closure should be considered if not routinely recommended when present for cryptogenic stroke.

Reassuringly, PFO closure is a safe procedure with low adverse event rates such as major bleeding and mortality similar to medical therapy including major bleeding and mortality combined and in individual studies [8–12]. The only exception was new onset atrial fibrillation being more common in the PFO closure group, statistically significant in three trials and when pooled [8,11–13]. This appears procedure-related, despite atrial fibrillation being not uncommon in cryptogenic stroke [24]. It appeared that studies of Amplatzer device had lower raw rates and didn't reach significance for atrial fibrillation compared to placebo [9,10,13], compared to studies of other devices [11,12]. The significance of this, including the closure device used and any additional stroke risk, is uncertain, however all studies reported most but not all the atrial fibrillation to be brief, non-sustained and/or occurring early post-procedure, with very few long-term complications including stroke [8–12].

This meta-analysis has several limitations. The heterogeneity in study inclusions, trial designs, characteristics, treatment particularly medical therapy and outcome definitions can affect and sometimes muddle the interpretation. Power remains suboptimal given the total number of studies and patients being moderate for interventional procedure analyses, particularly for low event outcomes such as mortality and adverse events as well as subgroup analysis. We did not have individual patient level data which would provide a more accurate picture as well as the ability to perform multivariate analysis more accurately. Loss to follow-up may present as bias to the effect size, especially in two trials exceeding 10% [8,13], as well as crossover. Follow-up duration was restricted to median of no more than 6 years and longer-term event rates are unknown. We also did not analyse cost-effectiveness data which is lacking in the literature.

In conclusion, pooling the findings from five randomised trials, percutaneous PFO closure significantly reduced ischaemic stroke and composite neurovascular or mortality

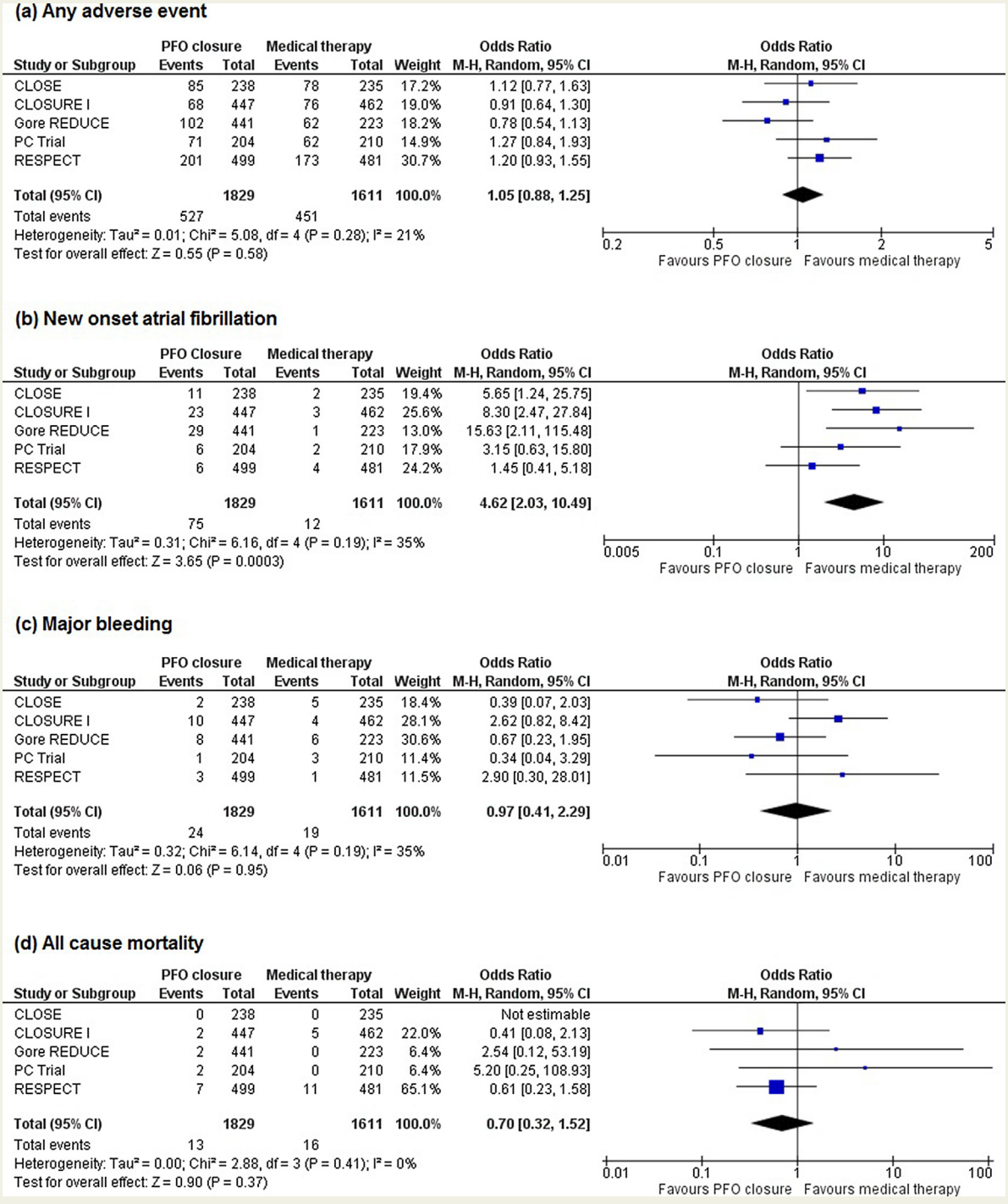

Figure 3 Safety Forest plot of odds ratio of (a) any adverse event, (b) new onset atrial fibrillation, (c) major bleeding and (d) all-cause mortality, in patients randomised to patent foramen ovale (PFO) closure and medical therapy.

Table 4 Sub-group analysis of the primary study outcome.

Subgroup	CLOSE		CLOSURE I		Gore Reduce		PC Trial		RESPECT		Total			
	PFO closure, no. (%)	Medical therapy, no. (%)	PFO closure, no. (%)	Medical therapy, no. (%)	PFO closure, no. (%)	Medical therapy, no. (%)	PFO closure, no. (%)	Medical therapy, no. (%)	PFO closure, no. (%)	Medical therapy, no. (%)	PFO closure, no. (%)	Medical therapy, no. (%)	Odds Ratio (95% CI)	P-value
Age ≤ 45 years	0/124 (0.0%)	5/112 (4.5%)	N/R	N/R	3/204 (1.5%)	6/114 (5/3%)	1/91 (1.1%)	6/97 (6.2%)	6/230 (2.6%)	10/210 (4.8%)	10/649 (1.5%)	27/323 (8.4%)	0.34 (0.16-0.71)	0.004
Age > 45 years	0/114 (0.0%)	9/123 (7.3%)	N/R	N/R	3/237 (1.3%)	6/109 (5.5%)	6/113 (5.3%)	5/113 (4.4%)	12/262 (4.6%)	18/266 (6.8%)	22/726 (3.0%)	38/611 (6.2%)	0.52 (0.22-1.23)	0.14
Male	0/137 (0.0%)	13/142 (9.2%)	7/208 (3.4%)	15/232 (6.8%)	3/261 (1.1%)	8/138 (5.8%)	N/R	N/R	10/268 (3.7%)	16/268 (6.0%)	20/874 (2.3%)	52/512 (10.2%)	0.23 (0.07-0.82)	0.02
Female	0/101 (0.0%)	1/93 (1.1%)	15/192 (7.9%)	14/219 (7.0%)	3/180 (1.7%)	4/85 (4.7%)	N/R	N/R	8/231 (3.5%)	12/213 (5.6%)	26/704 (3.7%)	31/610 (5.1%)	0.78 (0.44-1.37)	0.38
Atrial septal aneurysm	0/81 (0.0%)	9/74 (12.2%)	15/249 (6.2%)	20/291 (7.4%)	N/R	N/R	4/47 (8.5%)	2/51 (3.9%)	3/179 (1.7%)	13/170 (7.6%)	22/556 (4.0%)	44/595 (7.4%)	0.49 (0.14-1.74)	0.27
No atrial septal aneurysm	0/157 (0.0%)	5/161 (3.1%)	7/151 (4.6%)	9/160 (6.0%)	N/R	N/R	3/157 (1.9%)	9/159 (5.7%)	15/320 (4.7%)	15/311 (4.8%)	25/785 (3.2%)	38/791 (4.8%)	0.65 (0.33-1.29)	0.22
Large shunt size	0/157 (0.0%)	5/161 (3.1%)	10/231 (4.3%)	15/228 (6.6%)	4/348 (1.1%)	10/173 (5.8%)	N/R	N/R	13/247 (5.3%)	12/244 (4.9%)	27/983 (2.7%)	42/793 (5.3%)	0.47 (0.20-1.13)	0.09
Small shunt size	0/81 (0.0%)	9/74 (12.2%)	8/118 (6.9%)	10/155 (6.8%)	1/77 (1.3)	2/43 (4.7%)	N/R	N/R	5/247 (2.0%)	12/231 (6.9%)	14/523 (2.7%)	33/503 (6.6%)	0.41 (0.14-1.23)	0.11
Stroke index event	N/R	N/R	15/300 (5.1%)	15/324 (5.1%)	N/R	N/R	5/165 (3.0%)	8/163 (4.9%)	N/R	N/R	20/465 (4.3%)	23/487 (4.7%)	0.9 1 (0.49-1.69)	0.77
Transient ischaemic attack index event	N/R	N/R	7/100 (7.1%)	14/126 (11/6%)	N/R	N/R	2/39 (5.1%)	3/47 (6.4%)	N/R	N/R	9/139 (6.5%)	17/173 (9.8%)	0.64 (0.27-1.48)	0.30
Previous cardiovascular event	0/22 (0.0%)	2/23 (8.7%)	N/R	N/R	N/R	N/R	2/76 (2.6%)	6/79 (7.6%)	N/R	N/R	2/98 (2.0%)	8/102 (7.8%)	0.29 (0.07-1.24)	0.09
No previous cardiovascular event	0/216 (0.0%)	12/212 (5.7%)	N/R	N/R	N/R	N/R	5/128 (3.9%)	5/141 (3.8%)	N/R	N/R	5/344	17/353	0.25 (0.25-10.37)	0.46

Abbreviations: CLOSE, Patent Foramen Ovale Closure or Anticoagulants versus Antiplatelet Therapy to Prevent Stroke Recurrence; Gore REDUCE, GORE1 HELEX1 Septal Occluder / GORE1 CARDIOFORM Septal Occluder for Patent Foramen Ovale (PFO) Closure in Stroke Patients; RESPECT, Randomized Evaluation of Recurrent Stroke Comparing PFO Closure to Established Current Standard of Care Treatment.

events compared to medical therapy alone in cryptogenic stroke patients with PFO. The only adverse event higher in PFO closures was new atrial fibrillation suggesting it is a safe and effective procedure. The current evidence now favours undertaking PFO closure in cryptogenic stroke patients.

Conflict of Interest

No conflicts of interest, relationships with industry or grants to disclose for all authors.

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