Supplementary Material

Fully Biodegradable versus Nitinol Occluder Devices for Transcatheter Patent Foramen Ovale Closure: A Systematic Review

Supplementary Table S1. Risk of bias assessment of the randomized controlled trial using RoB 2

Study	D1	D2	D3	D4	D5	Overall	Main reason
Zhang et al. 2026	Low	Low	Low	Low	Some concerns	Some concerns	Prespecified statistical analysis plan was not clearly available

Supplementary Table S2. Risk of bias assessment of non-randomized comparative studies using ROBINS-I

Study	D1	D2	D3	D4	D5	D6	D7	Overall	Main concerns
Li et al. 2025	Serious	Moderate	Low	Low	Moderate	Moderate	Moderate	Serious	Retrospective design; possible confounding by device-selection factors, baseline anatomy, and migraine severity; single-center design; variable follow-up denominators
Sun et al. 2025	Serious	Serious	Low	Low	Moderate	Moderate	Moderate	Serious	Retrospective design; possible confounding; final analyzed cohort differed from initially enrolled cohort; incomplete standardization of follow-up and rhythm surveillance

Supplementary Table S3. GRADE-informed summary of findings and certainty of evidence

Outcome	No. of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Impact text	Certainty	Importance
Procedural success / implantation feasibility	3	1 randomized trial and 2 retrospective cohort studies	Serious	Not serious	Not serious	Serious	None	Procedural feasibility was high in both biodegradable and nitinol/metallic device groups. Zhang et al. reported successful implantation in 95/96 patients in the biodegradable group and 94/94 in the nitinol group. Li et al. reported successful implantation in 81/81 and 77/77 patients, respectively. In Sun et al., 56 biodegradable-device patients and 77 metallic-device patients were successfully implanted and completed follow-up; however, these figures represent the final analyzed cohort rather than a strict intention-to-treat procedural-success denominator. No pooled effect estimate was calculated because procedural-success definitions and denominators varied across studies.	**Low**	Important
Moderate-to-large residual shunt	3	1 randomized trial and 2 retrospective cohort studies	Serious	Serious	Not serious	Serious	None	Moderate-to-large residual shunt decreased over time in both groups, with no clear advantage for either device type. In Zhang et al., moderate-to-large residual shunt occurred in 9/96 versus 8/94 patients at 6 months and 5/96 versus 8/94 patients at 24 months. Li et al. reported 28/74 versus 27/71 at 6 months and 15/71 versus 12/68 at 12 months. Sun et al. reported declining rates from 1 to 12 months in both groups. No pooled effect estimate was calculated because imaging protocols, follow-up time points, and denominators varied.	**Low**	Important
Any residual shunt	2	2 retrospective cohort studies	Serious	Serious	Not serious	Serious	None	Any residual shunt was reported only in the cohort studies. In Li et al., any residual shunt occurred in 57/74 versus 55/71 patients at 6 months and decreased to 30/71 versus 24/68 at 12 months. In Sun et al., any residual shunt decreased from 12/52 versus 21/70 at 1 month to 8/38 versus 12/51 at 12 months. No pooled estimate was calculated because definitions and denominators varied.	**Very low**	Important
Serious adverse events	3	1 randomized trial and 2 retrospective cohort studies	Serious	Not serious	Not serious	Very serious	None	Serious adverse events were rare in both device groups. In the randomized trial, one serious adverse event occurred in the biodegradable group requiring surgical removal, and one occurred in the nitinol group involving femoral vein puncture-site bleeding. No serious adverse events were reported in either retrospective cohort. The evidence base was too small to exclude clinically important differences in rare harms.	**Very low**	Critical
Atrial fibrillation / atrial flutter or clinically detected arrhythmia	3	1 randomized trial and 2 retrospective cohort studies	Serious	Serious	Not serious	Very serious	None	AF/AFL events were uncommon. The randomized trial reported no AF/AFL events through early follow-up and 6 months. Li et al. reported transient AF in 3/81 biodegradable-device patients and 2/77 nitinol-device patients. Sun et al. reported no AF/AFL in either arm, based on short-term ECG monitoring. Certainty was limited because rhythm monitoring was not standardized and transient arrhythmias may have been under-detected.	**Very low**	Critical
Device thrombosis	3	1 randomized trial and 2 retrospective cohort studies	Serious	Not serious	Not serious	Very serious	None	No device thrombosis was reported in any included study. However, the total sample size was small and follow-up/surveillance methods varied, so absence of observed events does not exclude rare device-thrombosis risk.	**Very low**	Critical
Embolization, malposition, detachment, or reintervention	3	1 randomized trial and 2 retrospective cohort studies	Serious	Serious	Not serious	Very serious	None	Embolization, malposition, detachment, or reintervention events were uncommon. Li et al. reported one biodegradable-device detachment and no events in the nitinol group. Zhang et al. reported one biodegradable-device case requiring surgical removal because of intraprocedural deformation. Zhang et al. and Sun et al. reported no embolization or malposition cases.	**Very low**	Critical

								Certainty was very low because events were rare, definitions varied, and the evidence base was underpowered for uncommon procedural complications.		
Mortality and recurrent stroke/TIA	2–3	1 randomized trial and 1–2 retrospective cohort studies with extractable or partially extractable data	Serious	Serious	Serious	Very serious	None	Mortality and recurrent neurological events were rare or inconsistently reported. The randomized trial reported no deaths in either group. Li et al. reported no recurrent stroke or TIA at 12 months in either group. Sun et al. did not provide extractable stroke/TIA recurrence data. Certainty was very low because event counts were extremely small, reporting was incomplete, and the evidence combined one mixed-indication RCT with migraine-specific cohorts.	**Very low**	Critical
Migraine outcomes	2	2 retrospective cohort studies	Serious	Serious	Serious	Serious	None	Migraine outcomes improved in both device groups, but no clear between-device difference was demonstrated. Sun et al. reported no significant difference in postoperative MIDAS score or monthly migraine attack days between biodegradable and metallic occluders at 12 months. Li et al. also reported significant postoperative improvement in both groups, with no significant between-device difference in migraine relief by Kaplan–Meier analysis. Certainty was very low because both studies were retrospective, outcome reporting was not fully comparable, and no randomized migraine-specific comparison was available.	**Very low**	Important

Supplementary Table S4. Full electronic search strategies

MEDLINE (EBSCOhost) 39

((MH "Foramen Ovale, Patent+") OR TI ("patent foramen ovale" OR PFO OR "interatrial shunt") OR AB ("patent foramen ovale" OR PFO OR "interatrial shunt"))

AND

(TI (closure OR occlud* OR device* OR transcatheter OR percutaneous OR catheter*) OR AB (closure OR occlud* OR device* OR transcatheter OR percutaneous OR catheter*))

AND

(TI (biodegrad* OR bioabsorb* OR absorbable OR resorbable OR polydioxanone OR PDO OR PLLA OR polylact* OR "poly l lactic" OR "poly(L-lactic acid)" OR MemoSorb)

OR AB (biodegrad* OR bioabsorb* OR absorbable OR resorbable OR polydioxanone OR PDO OR PLLA OR polylact* OR "poly l lactic" OR "poly(L-lactic acid)" OR MemoSorb))

PubMed 40

(("Foramen Ovale, Patent"[Mesh] OR "patent foramen ovale"[tiab] OR PFO[tiab] OR "interatrial shunt"[tiab])

AND

(closure[tiab] OR occlud*[tiab] OR device*[tiab] OR transcatheter[tiab] OR percutaneous[tiab] OR catheter*[tiab])

AND

(biodegrad*[tiab] OR bioabsorb*[tiab] OR absorbable[tiab] OR resorbable[tiab]

OR polydioxanone[tiab] OR PDO[tiab]

OR PLLA[tiab] OR polylact*[tiab] OR "poly l lactic"[tiab] OR "poly(L-lactic acid)"[tiab]

OR MemoSorb[tiab]))

Embase 77

('patent foramen ovale'/exp OR 'patent foramen ovale' OR 'patent foramen ovale':ti,ab,kw OR pfo:ti,ab,kw OR 'interatrial shunt':ti,ab,kw) AND (closure:ti,ab,kw OR occlud*:ti,ab,kw OR device*:ti,ab,kw OR transcatheter:ti,ab,kw OR percutaneous:ti,ab,kw OR catheter*:ti,ab,kw) AND (biodegrad*:ti,ab,kw OR bioabsorb*:ti,ab,kw OR absorbable:ti,ab,kw OR resorbable:ti,ab,kw OR polydioxanone:ti,ab,kw OR pdo:ti,ab,kw OR plla:ti,ab,kw OR polylact*:ti,ab,kw OR 'poly l lactic':ti,ab,kw OR 'poly(l-lactic acid)':ti,ab,kw OR memosorb:ti,ab,kw)

Scopus 71

TITLE-ABS-KEY(("patent foramen ovale" OR pfo OR "interatrial shunt") AND (occlud* OR closure OR device* OR transcatheter OR percutaneous OR catheter*) AND (biodegrad* OR bioabsorb* OR absorbable OR resorbable OR polydioxanone OR PDO OR PLLA OR polylact* OR "poly l lactic" OR MemoSorb))

Cochranelibrary 120

#1 [mh "Foramen Ovale, Patent"]

#2 ("patent NEXT foramen NEXT ovale" OR PFO OR "interatrial NEXT shunt" OR "right-to-left NEXT shunt"):ti,ab,kw

#3 #1 OR #2

#4 (occlud* OR closure OR device* OR transcatheter OR percutaneous OR (septal NEXT occlud*)):ti,ab,kw

#5 #3 AND #4

Web of Science 61

TS=(("patent foramen ovale" OR PFO OR "interatrial shunt") AND (occlud* OR closure OR device* OR transcatheter OR percutaneous OR catheter*) AND (biodegrad* OR bioabsorb* OR absorbable OR resorbable OR polydioxanone OR PDO OR PLLA OR polylact* OR "poly l lactic" OR memsorb))

ClinicalTrials.gov

Condition or disease: `Patent Foramen Ovale`

Other terms (copy/paste): `biodegradable OR bioabsorbable OR absorbable OR resorbable OR polydioxanone OR PDO OR PLLA OR polylactic OR MemoSorb OR nitinol`

WHO ICTRP

Search 1

`"patent foramen ovale" biodegradable`

Search 2

`PFO bioabsorbable occluder`

Search 3

`"patent foramen ovale" (PDO OR PLLA OR polydioxanone OR polylactic OR MemoSorb)`

Supplementary Table S5. Patient flow across included studies (enrolled → implanted → evaluable at each imaging time point)

Study (design)	Group	Enrolled / randomized	Implanted	Evaluable at follow-up imaging
Zhang et al. (RCT)	Biodegradable	96	95	96 at 6 mo; 96 at 24 mo (ITT)
Zhang et al. (RCT)	Nitinol	94	94	94 at 6 mo; 94 at 24 mo (ITT)
Li et al. (cohort)	Biodegradable	83	81	74 at 6 mo; 71 at 12 mo
Li et al. (cohort)	Nitinol	81	77	71 at 6 mo; 68 at 12 mo
Sun et al. (cohort)	Biodegradable	60	56	52 at 1 mo; 45 at 6 mo; 38 at 12 mo

Sun et al. (cohort)	Metallic	85	77	70 at 1 mo; 63 at 6 mo; 51 at 12 mo

ITT, intention-to-treat. Zhang et al. analysed all randomised patients under ITT, so denominators were stable across follow-up. Li et al. screened 168 patients → 164 allocated → 158 analysed (6 excluded: nitinol group 3 massive cerebral infarction and 1 participation in another trial; biodegradable group 2 massive cerebral infarction). Sun et al. enrolled 145 patients → 133 analysed (biodegradable 60→56: 1 declined the procedure, 3 lost to follow-up; metallic 85→77: 2 intraprocedural pericardial tamponade, 1 procedure aborted for failed guidewire crossing, 5 lost to follow-up). The proportion of patients without follow-up imaging at the final time point was similar between device groups within each cohort (Li et al. 12.3% vs 11.7%; Sun et al. 32.1% vs 33.8%), i.e. attrition was non-differential between device types.

Supplementary Table S6. Right-to-left shunt grading scales and residual-shunt definitions across studies

Parameter	**Zhang et al.**	**Li et al.**	**Sun et al.**
Imaging modality	Contrast echocardiography (Valsalva)	Contrast TTE (cTTE, Valsalva)	Contrast TEE / TTE
Grading scale	RLS grade 1–3	RLS grade 0–III	Grade II vs Grade III+
Effective / successful closure	RLS grade 0–1	RLS grade 0–1	—
Moderate-to-large residual (Table 3A)	Grade 2–3 (“unsuccessful closure”)	Grade II–III	Grade II (on follow-up)
Baseline inclusion threshold	Grade II–III / high-risk PFO	Grade II–III	Grade II or higher

RLS, right-to-left shunt; TTE, transthoracic echocardiography; cTTE, contrast TTE; TEE, transoesophageal echocardiography. The between-study spread in moderate-to-large residual-shunt rates (approximately 7–11% in Zhang and Sun versus approximately 38% in Li at 6 months) is largely attributable to these differing definitions, imaging modalities, and grading thresholds rather than to device performance.