UNIVERSITÄT LEIPZIG

Universitätsklinikum Leipzig
Klinik und Poliklinik für Kardiologie

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HERZZENTRUM LEIPZIG

Pulmonary Vein Isolation versus SHAM-pulmonary vein isolation for symptomatic relief in patients with Atrial Fibrillation

- the PVI-SHAM-AF trial

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DISCLOSURES

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This trial was funded by Helios Gesundheit, a large European hospital group, under the programme Förderung Leipziger Herzmedizin, and Leipzig University was the legal sponsor.

BACKGROUND

- Guidelines recommend catheter ablation by pulmonary vein isolation (PVI) to reduce symptoms in paroxysmal and persistent atrial fibrillation (AF)

- Previous RCTs evaluating symptom relief lack a sham-control or sufficient sample size leaving potential placebo-effects insufficiently explored

Van Gelder et al., Eur Heart J 2024 29;45(36):3314-3414 | Mark et al., JAMA 2019;321:1275-1285
Dulai et al., JAMA 2024;332:1165-1173 | Osmancik et al., Circulation 2026;153

TRIAL DESIGN

PVI-SHAM-AF

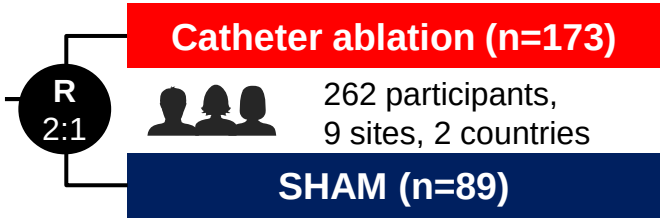
Multicentre, double-blind, sham-controlled investigator-initiated trial

Key inclusion criteria

Symptomatic AF
Indication for catheter ablation by ESC guidelines

Key exclusion criteria

History of previous PVI
Left ventricular ejection fraction <35%



Sample size

Projected 260 patients

Expected: Difference of 8 points in AFEQT summary score (SD 20 points)

Assuming 10% dropouts
80% power, 2-sided α = 0.05

Follow-up time (median, IQR): 184 days (181;191)

PRIMARY OUTCOME

Between-group difference in change from baseline to 6 months in the Atrial Fibrillation Effect on the Quality-of-life Questionnaire (AFEQT) summary score

SECONDARY OUTCOMES

Longitudinal change in AFEQT score from baseline to months 3 and 6
Change in EQ-5D-3L and SF-36 from baseline to months 3 and 6
AF burden during 7-day Holter ECG monitoring at 6 months
Incidence of AF recurrence after 3 and 6 months

SAFETY ASSESSMENT

All serious adverse events were blindly adjudicated for related or possibly related to the study procedure

Dilk et al., Am Heart J 2025;290:93-104 | Hindricks et al. Eur Heart J 2021;42:373-498

SHAM INTERVENTION

PVI-SHAM-AF

All patients were hospitalized for the study procedure

1 — 2 — 3 — 4

1 Preparation and Sedation

Analgosedation for ≥60 minutes according to local standard for PVI.

Noise-reducing headphones with piano music for acoustic isolation.

2 Vascular Access

Two venous punctures in the femoral vein (typically with 6F sheaths).

5000 IU unfractionated heparin administered.

3 Sham Procedure

No catheter was placed.

No transseptal puncture.

No ablation.

No fluoroscopy.

4 Cardioversion (if required)

Electrical cardioversion performed if the patient was in AF at the end of the procedure, as per protocol.

SHAM INTERVENTION

PVI-SHAM-AF

All patients were hospitalized for the study procedure

Patient and physicians blinded

1 — 2 — 3 — 4 — 5 — 6

1 Preparation and Sedation

Analgosedation for ≥60 minutes according to local standard for PVI.

Noise-reducing headphones with piano music for acoustic isolation.

2 Vascular Access

Two venous punctures in the femoral vein (typically with 6F sheaths).

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5 Post-Procedural Care

Standard post-procedural monitoring and care, indistinguishable from PVI patients.

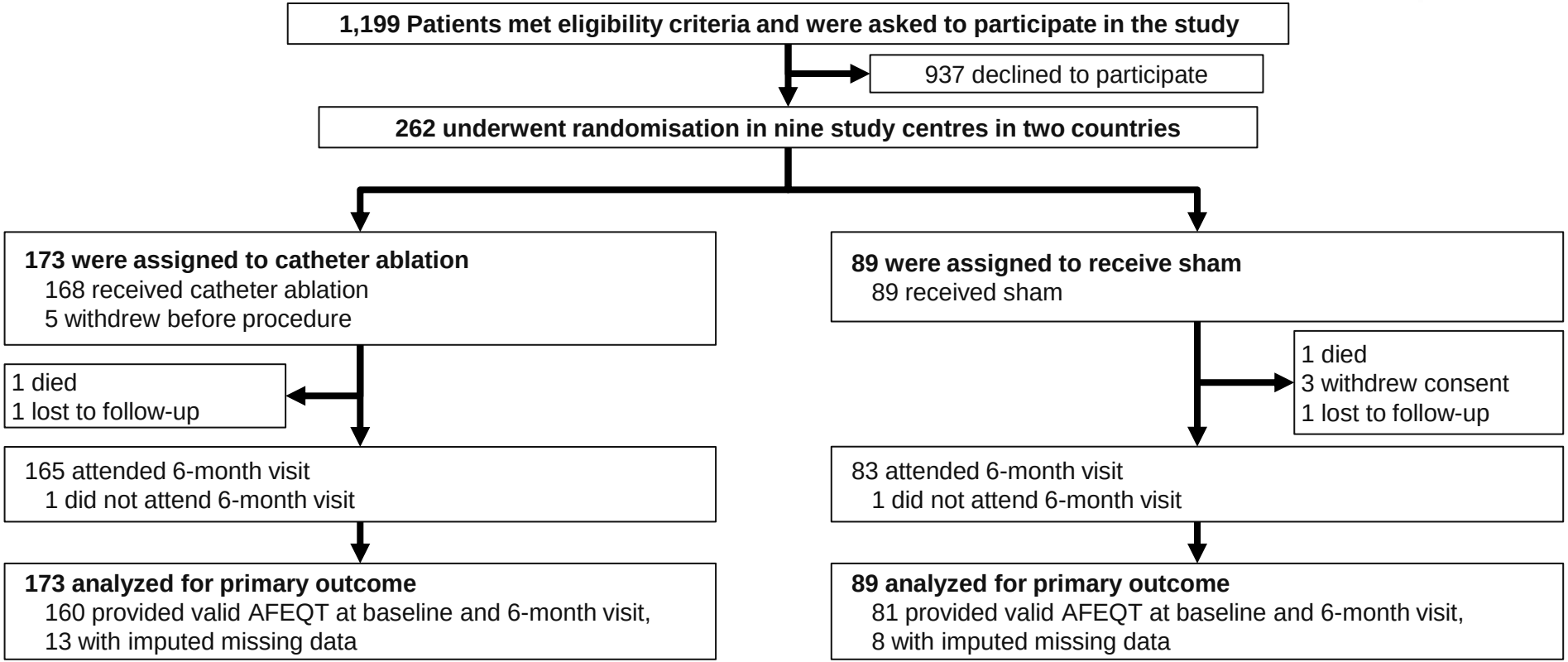
Clinical report does not specify allocation.

6 Medications

Antiarrhythmic drugs managed according to protocol and clinical judgment.

Oral anticoagulation continued.

CONSORT DIAGRAM



BASELINE CHARACTERISTICS	CATHETER ABLATION (n=173)	SHAM (n=89)
Age - years, median (IQR)	67 (62-73)	69 (63-73)
Female sex - n (%)	78 (45)	56 (63)
Body mass index – kg/m², median (IQR)	29 (26-33)	30 (27-34)
Medical history – n (%)		
Arterial hypertension	156 (90)	79 (89)
Diabetes mellitus	39 (23)	24 (27)
Coronary artery disease	34 (20)	11 (13)
Heart failure	23 (13)	15 (17)
Stroke	10 (6)	1 (1)
Type of AF– n (%)		
Paroxysmal	79 (46)	49 (55)
Persistent	94 (54)	40 (45)
Time since first AF diagnosis – years, median (IQR)	1.3 (0.4-4.0)	1.4 (0.4-4.1)
Baseline AFEQT score – median (IQR)	61 (46-77)	61 (44-75)

PROCEDURAL CHARACTERISTICS	CATHETER ABLATION (n=173)	SHAM (n=89)
Ablation modality – n (%) Radiofrequency Cryoballoon Pulsed field ablation	 103 (61) 57 (35) 8 (5)	NA
Duration of analgosedation – min (mean, SD)	90±32	75±17
Venous sheaths – n (mean, SD)	2.2±0.4	1.7±0.4
Direct current cardioversion - n (%)	90 (54)	32 (36)
Cumulative doses, all given i.v. – mg (median, IQR) Propofol Midazolam Fentanyl	 482 (359-643) 3.0 (3.0-4.0) 0.075 (0.075-0.125)	 342 (270-460) 3.0 (3.0-4.5) 0.025 (0.025-0.050)

Five patients out of 173 in the catheter ablation group did not receive the PVI procedure.

PULMONARY VEIN ISOLATIONS WITHIN 6 MONTHS IN VIOLATION OF THE STUDY PROTOCOL

	CATHETER ABLATION (n=173)	SHAM (n=89)
Pulmonary vein isolation – n (days after randomisation)	2 (42,149)	2 (22,99)

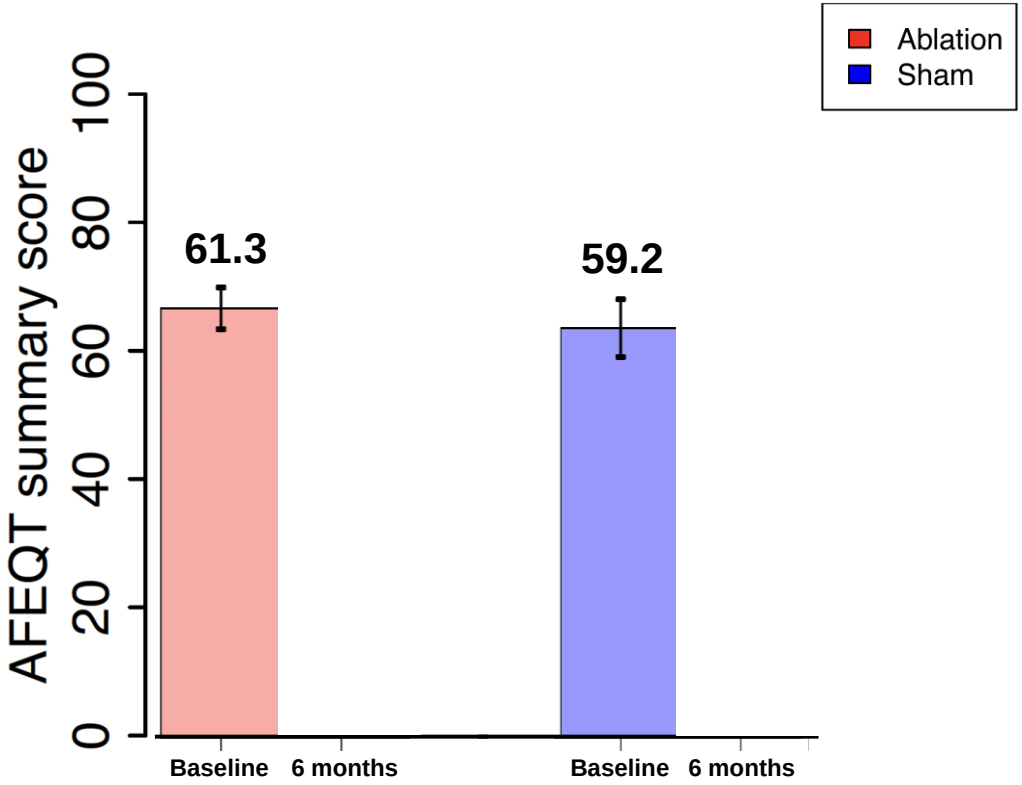
ASSESSMENT OF BLINDING

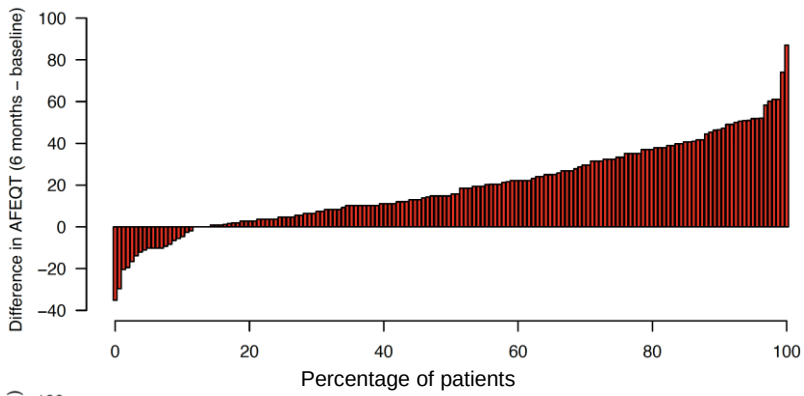
was performed after the procedure, before discharge.

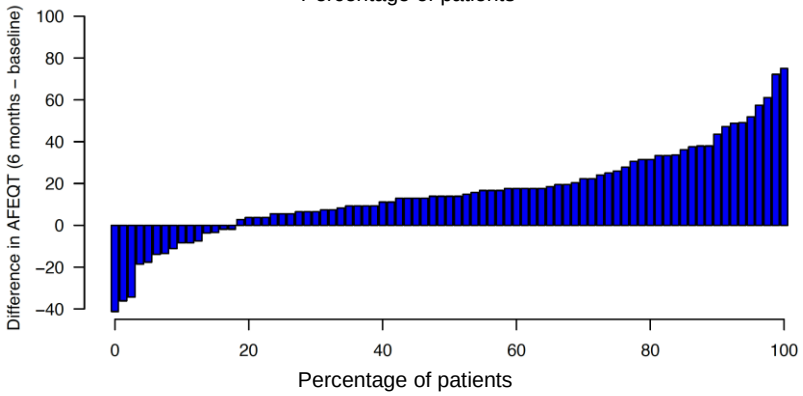
The simple blinding index for patients was 0.06 (95% CI -0.07 to 0.19, p=0.40), results that indicated that the blinding strategy was effective.

Petroff et al., Contemp Clin Trials Commun. 2024 Nov 26:42:101393

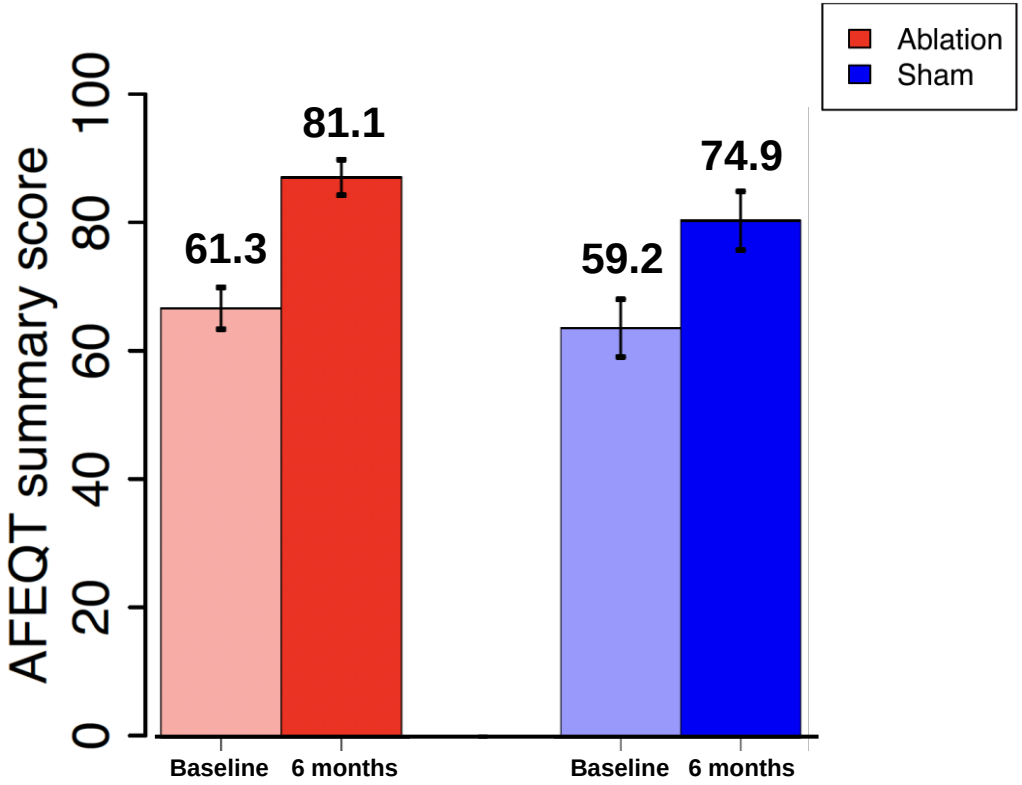
PRIMARY OUTCOME: AF-RELATED QUALITY OF LIFE BY CHANGE IN AFEQT SUMMARY SCORE 6 MONTHS TO BASELINE







PRIMARY OUTCOME: AF-RELATED QUALITY OF LIFE BY CHANGE IN AFEQT SUMMARY SCORE 6 MONTHS TO BASELINE



Adjusted between-group difference
(Hodges-Lehman estimate)

2.6 points

95% CI −2.7 to 8.0; p=0.36

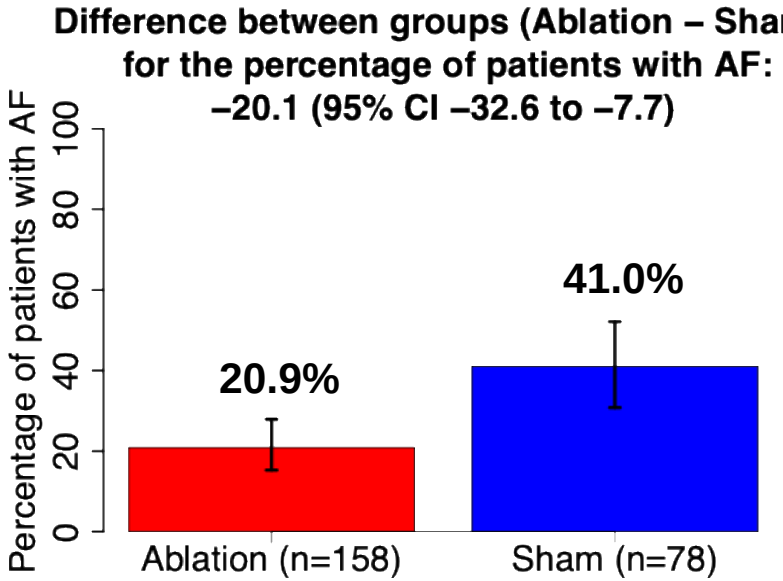
No statistically significant benefit of ablation for the prespecified AFEQT primary endpoint at 6 months

PRIMARY AND SECONDARY OUTCOMES

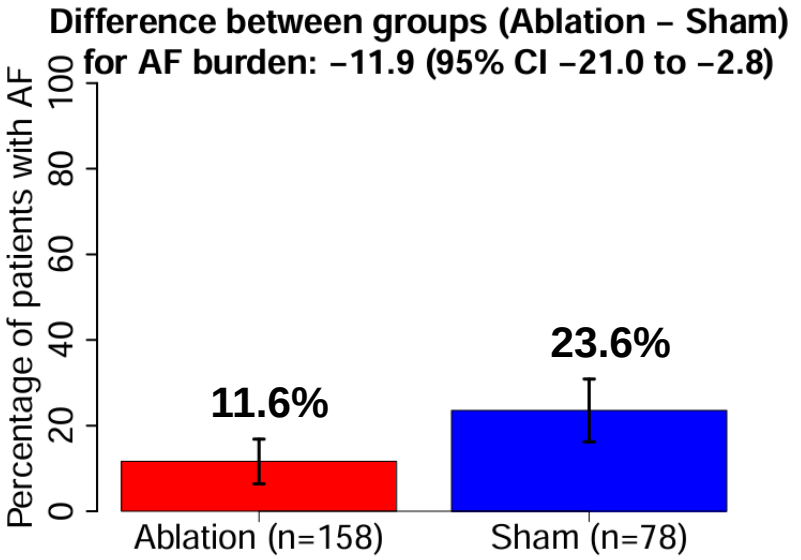
	CATHETER ABLATION mean (SD)	SHAM mean (SD)	Treatment effect (95% CI)
AFEQT summary score (Primary endpoint)	19.0 (20.5)	14.5 (21.7)	2.6 (-2.7 to 8.0)
AFEQT subscales			
Symptoms	19.0 (25.8)	13.8 (23.6)	5.5 (0.4 to 10.6)
Daily activities	20.6 (27.2)	17.9 (28.1)	6.0 (0.2 to 11.7)
Treatment concerns	16.1 (20.6)	14.2 (22.9)	3.8 (-0.9 to 8.4)
Treatment satisfaction	19.5 (26.0)	8.8 (26.3)	7.8 (2.0 to 13.6)
SF-36 Physical functioning	6.8 (16.7)	7.9 (21.1)	1.1 (-3.3 to 5.5)
EQ-5D-3L			
Index Score (TTO method)	−0.012 (0.015)	-0.024 (0.204)	0.014 (-0.024 to 0.052)
Visual Analogue Scale (VAS)	8.7 (18.4)	5.9 (19.4)	3.8 (-0.2 to 7.8)

SECONDARY OUTCOMES: AF RECURRENCE AND AF BURDEN IN 7-DAY HOLTER ECG

AF RECURRENCE



AF BURDEN



SAFETY

2 Deaths (non-procedure related)

- † CATHETER ABLATION group: Intracranial haemorrhage, 85 days after procedure
- † SHAM group: Brain cancer, 101 days after procedure

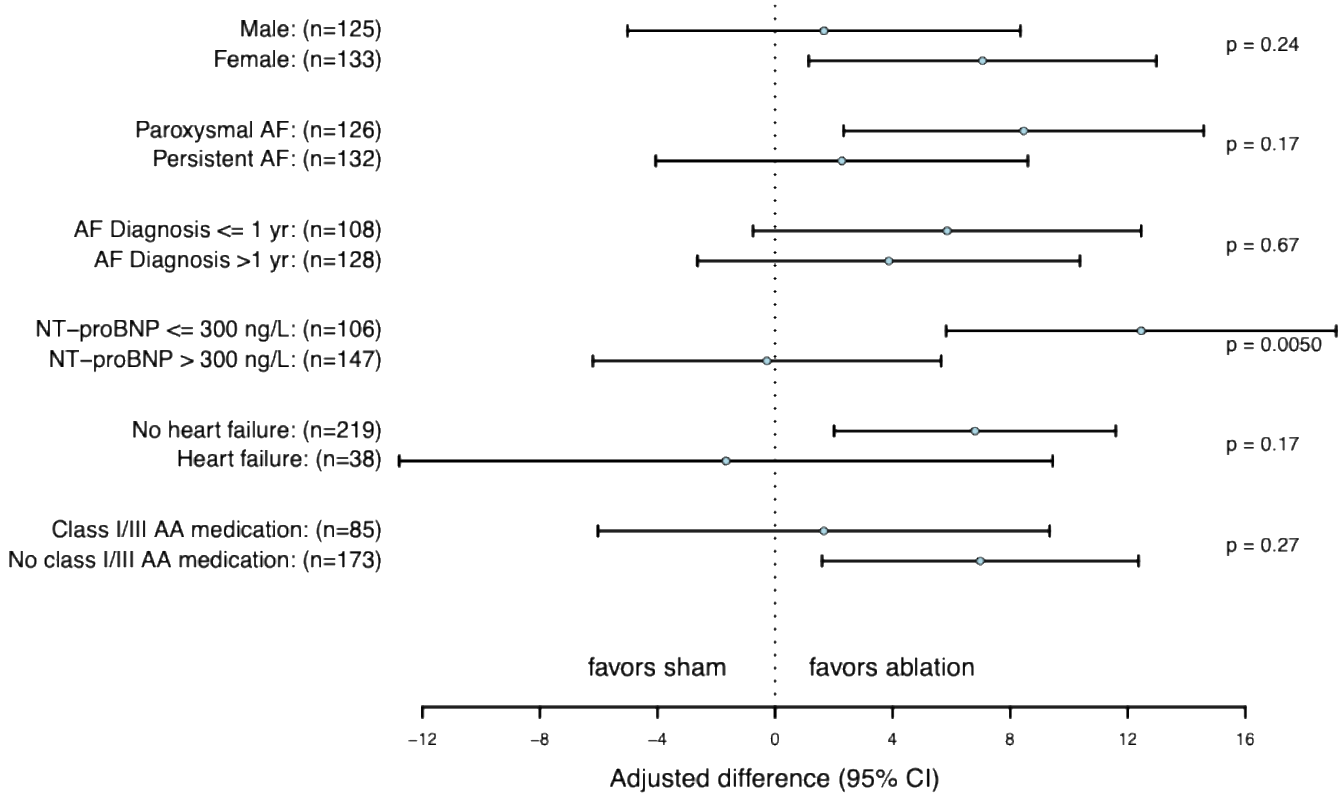
1 Ischemic stroke (procedure and AF related)

- SHAM group: 2 days after procedure (including electrical cardioversion)

5 Vascular access complications (procedure related)

- 3 CATHETER ABLATION group – all treated locally
- 2 SHAM group: one treated locally, one by interventional selective embolisation

SUBGROUP ANALYSIS FOR PRIMARY ENDPOINT



LIMITATIONS

- 22% of invited patients gave informed consent which limits generalizability, presumably inevitable when a procedure is available in routine care
- No assessment of AF burden at baseline
- Only 5% of patients received pulsed field ablation
- AF recurrence may be underestimated as we did not use continuous ECG monitoring
- Study included primarily white population in Germany and Poland
- 6 months may be too short for catheter ablation to induce improvement in quality of life → follow-up of PVI-SHAM-AF is ongoing

CONCLUSIONS

- In this double-blind, multicentre, sham-controlled trial, catheter ablation and the active sham procedure showed symptomatic improvement in the AFEQT summary score at 6 months, but catheter ablation did not demonstrate superiority
- Catheter ablation was safe and reduced the percentage of patients with AF and AF burden after 6 months
- Symptomatic improvement observed after ablation and improvement in AF recurrences/burden are distinct and symptomatic improvement cannot necessarily be attributed entirely to the ablation procedure
- Sham-controlled trials for well established cardiovascular procedures are feasible and provide important information

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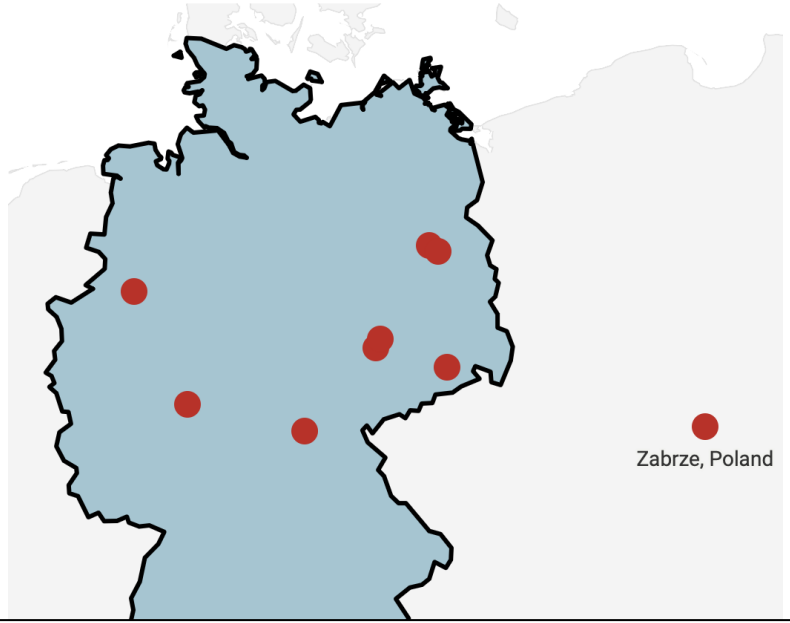

Funding provided by HELIOS through programme „Förderung Leipziger Herzmedizin“ and Leipzig University was the formal sponsor

262 patients who participated in this study

FOR FURTHER DETAILS…

THE LANCET

Catheter ablation for symptomatic atrial fibrillation (PVI-SHAM-AF): a randomised, double-blind, sham-controlled, multicentre trial

Rolf Wachter, Patrick Haag, Tobias Uhe, Miroslav Bacak, David Petroff, Mathias Forkmann, Lars Eckardt, Thomas Gaspar, Borislav Dinov, Martin Neef, Kerstin Bode, Timm Seewöster, Sotirios Nedios, Sebastian Hilbert, Matthias Lerche, Frank Lindemann, Christian Spies, Samira Beimel, Beatriz Tose Costa Paiva, Felix Hohendanner, Verena Tscholl, Radosław Lenarczyk, Leonard Bergau, Christian Sohns, Christiane Prettin, Ulrich Laufs, Gerhard Hindricks, Nikolaos Dagres, for the PVI-SHAM-AF Investigators