ESC European Society of Cardiology

Europace (2025) **27**, euaf110
https://doi.org/10.1093/europace/euaf110

META-ANALYSIS

Impact of catheter ablation timing according to duration of atrial fibrillation history on arrhythmia recurrences and clinical outcomes: a meta-analysis

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Received 7 April 2025; accepted after revision 24 May 2025; online publish-ahead-of-print 28 May 2025

Aims Catheter ablation is a well-established treatment for symptomatic paroxysmal atrial fibrillation (PAF) or persistent atrial fibrillation (PsAF) refractory to antiarrhythmic agents, and current guidelines have also upgraded its role as a first-line option for recurrent PAF. However, the optimal timing to maximize rhythm outcomes remains uncertain. To address this gap, the present study sought to investigate the association between diagnosis-to-ablation time (DAT) and age-stratified atrial fibrillation (AF) recurrence and clinical outcomes.

Methods and results Medline, the Cochrane Library, and Scopus were searched through 18 February 2025. Triple-independent selection, extraction, and quality assessment were conducted, with evidence pooled via random-effects meta-analyses. Among the 28 studies (41 431 participants) with a median 24-month follow-up, early ablation (DAT ≤ 1 year) significantly reduced AF recurrence compared to delayed ablation [hazard ratio (HR) 0.65, 95% confidence interval (CI) 0.59–0.73]. The benefit of early ablation was consistent for both PAF (HR 0.72, 95% CI 0.67–0.77) and PsAF (HR 0.70, 95% CI 0.61–0.81). Age-stratified analysis revealed that this effect was significant regardless of age, with the greatest risk reduction observed in individuals ≤ 55 years (HR 0.49, 95% CI 0.34–0.71). Early ablation was also associated with a reduced risk of repeat ablation, new cardioversion, and cardiovascular hospitalization compared to delayed ablation. Higher CHA_2DS_2-VASc scores, heart failure prevalence, and lower mean left ventricular ejection fraction were associated with greater benefits from early ablation.

Conclusion Early catheter ablation within 1 year of AF diagnosis is associated with a lower risk of recurrence in both PAF and PsAF, with the strongest association observed in patients ≤ 55 years.

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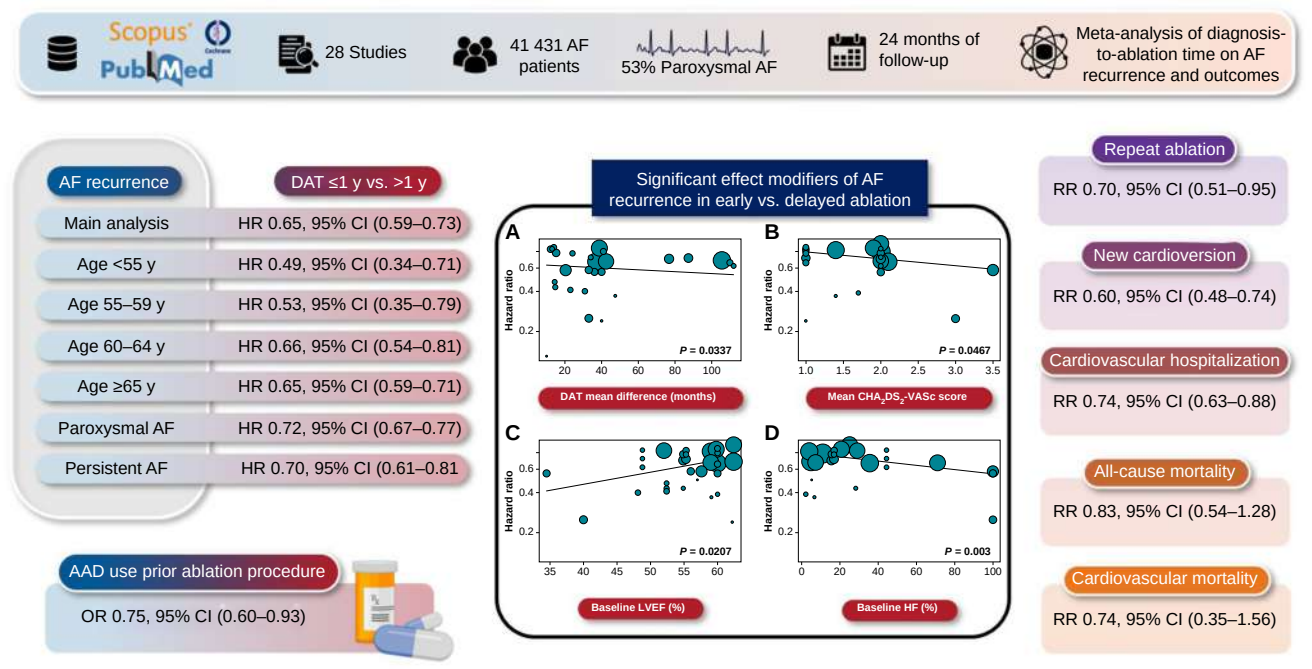
Graphical Abstract



Keywords Atrial fibrillation • Ablation timing • Diagnosis-to-ablation time • AF recurrence • Repeat ablation

Introduction

Atrial fibrillation (AF) is the most prevalent cardiac arrhythmia and a major determinant of morbidity and mortality.[1–5] Its incidence is projected to rise significantly in the coming years, imposing a substantial economic and logistical burden on healthcare systems.[6] Despite advancements in management, optimizing rhythm control strategies remains a persistent challenge.[7,8] Early therapeutic intervention is considered beneficial, as AF induces progressive atrial fibrosis, a key driver of atrial remodelling that is closely linked to disease perpetuation.[9,10] As structural remodelling advances, the efficacy of rhythm control therapies declines, underscoring the critical importance of timely intervention.[11]

Emerging evidence suggests that catheter ablation for AF confers superior efficacy in maintaining freedom from atrial arrhythmia recurrence and alleviating AF-related symptoms compared to antiarrhythmic drug (AAD) therapy, particularly in patients with paroxysmal AF (PAF).[12–16] Moreover, the adoption of catheter ablation as first-line treatment in PAF has been associated with a reduced likelihood of progression to persistent AF (PsAF) when compared to AAD, further supporting its role as a preferred therapeutic approach.[17,18] However, a closer examination of the inclusion criteria in these randomized controlled trials (RCTs) reveals that patient selection was largely limited to those with a prolonged history of AF, typically exceeding 6 months, and documented recurrent episodes.[13–20] Although AF frequency and burden were reported differently across studies, the overall burden was substantial, with a considerable proportion of participants having previously undergone cardioversion. Importantly, these trials did not encompass individuals presenting with an initial episode of AF, thereby limiting the applicability of their findings to early-stage disease and leaving the potential benefits of catheter ablation in newly diagnosed patients largely unexplored.

This gap in evidence raises critical questions regarding the optimal timing of ablation relative to timing of AF diagnosis. While current guidelines support early intervention in selected patients, long-term data on the efficacy and safety of an early ablation strategy in real-world clinical practice remain limited. Additionally, whether the benefits of early intervention extend uniformly across different age groups remains an area of ongoing debate. Given these uncertainties, the present study aimed to evaluate the impact of diagnosis-to-ablation time (DAT) on age-stratified AF recurrence and associated clinical outcomes.

Material and methods

This study was conducted in accordance with the methodological principles set forth in the Cochrane Handbook for Systematic Reviews,[21] with its reporting aligned with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines.[22] The protocol was preregistered on the Open Science Network (DOI 10.17605/OSF.IO/BMJYC) and was followed without modifications.

Search strategy

The search strategy was developed by two researchers (P.K. and N.F.), while a comprehensive and independent literature search was conducted by three researchers across MEDLINE (via PubMed), Scopus, and the Cochrane Database of Systematic Reviews, from inception to 18 February 2025. No restrictions were imposed regarding date, language, publication status, or year. The search strings incorporated both free-text and Medical Subject Headings (MeSH) terms, including atrial fibrillation, ablation, and diagnosis-to-ablation time. To enhance the breadth of the search, additional sources were explored, including manual searches of clinicaltrials.gov, the Epistemonikos database, and Google Scholar. Additionally, backward and forward citation tracking

was performed using the citationchaser R package.[23] The complete search strategy is detailed in Supplementary material online, *Tables S1–S3*.

Eligibility criteria

Inclusion criteria

Eligible studies included RCTs and observational studies that examined the relationship between DAT and post-ablation outcomes in adults (≥18 years) with AF.

Exclusion criteria

Studies with the following characteristics were excluded: (i) case reports, case series, and narrative reviews; (ii) editorials, letters, commentaries, and expert opinions; (iii) clinical practice guidelines, conference abstracts, study protocols, and dissertations; and (iv) cross-sectional studies, case-control studies, and crossover trials.

Outcomes

The primary endpoint of the meta-analysis was the comparative risk of AF recurrence between individuals undergoing early vs. late referral for first-time AF catheter ablation. Secondary outcomes included post-ablation cardioversion, repeat ablation, all-cause mortality, cardiovascular mortality, cardiovascular hospitalization, and serious periprocedural adverse events, as defined in the original studies. Early ablation was classified as a DAT of ≤1 year, while late ablation was defined as a DAT exceeding 1 year. This threshold was chosen based on its widespread use in primary literature and the findings of the only available RCT, which reported no significant difference in AF recurrence between ablation at 1 month and 12 months.[24]

Study selection

In the initial screening phase, three authors independently assessed the titles and abstracts of all records retrieved through the predefined search strategy. To maximize the sensitivity of study selection, no studies were excluded solely based on discrepancies at this stage. Full-text evaluations were then conducted independently by the same three investigators. Any disagreements were adjudicated through consensus or, when necessary, resolved in consultation with a senior author. The screening process was facilitated by Abstrackr,[25] while Mendeley was employed for reference management.

Data extraction

A structured data extraction form was developed and refined through a pilot phase involving a subset of four studies. Following iterative training and calibration exercises, a standardized form was finalized to ensure consistency and accuracy. Data extraction was conducted independently by three investigators, with discrepancies adjudicated through consensus or, when necessary, consultation with a senior author.

For each included study, extracted variables encompassed two broad domains: (i) study-specific details—study design, country, total number of patients with AF, AF subtype, type of catheter ablation, additional ablations, classification as first or repeat ablation, DAT stratification, definition of AF recurrence, blanking period, main inclusion criteria, primary outcome, and follow-up duration and (ii) baseline patient characteristics—group-specific sample size, percentage of male participants, mean age, body mass index (BMI), DAT, CHA_2DS_2-VASc score, left atrial diameter (LAD), history of prior cardioversion, left ventricular ejection fraction (LVEF), AF subtype (paroxysmal or persistent), and comorbidities, including heart failure, hypertension, diabetes, dyslipidaemia, obesity, coronary artery disease, obstructive sleep apnoea (OSA), and prior stroke.

Where necessary, corresponding authors of the original studies were contacted to obtain additional subgroup-level data that were either missing or not explicitly reported in the published manuscripts.

Quality assessment

The methodological quality of the included studies was rigorously appraised by two independent reviewers using the Risk of Bias in Non-Randomized Studies of Interventions (ROBINS-I) tool,[26] a comprehensive framework designed to evaluate the risk of bias in observational epidemiological research. Any discrepancies in assessment were addressed through deliberation, with unresolved differences adjudicated by a third reviewer when necessary.

Data analysis

All statistical analyses were conducted using R Statistical Software (v. 4.2). Hazard ratios (HRs) and count data for the predefined endpoints were extracted, with the early ablation group (DAT ≤ 1 year or ≤3 years) serving as the numerator and the late ablation group (DAT > 1 year or >3 years, respectively) as the reference. In instances where HR estimates were not directly reported, binomial data were transformed into HRs using established methodological approaches,[27] consistent with the validated framework applied in our prior meta-analysis on AF-related outcomes.[28]

Effect estimates, along with their 95% confidence intervals (CIs), were synthesized using three-level random-effects models, employing a restricted maximum likelihood estimator to account for between-study variance within a frequentist framework. Given that some studies reported distinct effect estimates corresponding to different DAT thresholds beyond 1 year (e.g. 1–3 years and >3 years), three-level meta-analytical models were implemented to accommodate this inherent dependency, assuming that effect sizes were hierarchically structured within individual studies. A two-tailed $P < 0.05$ was considered statistically significant for pooled effect estimates.

Heterogeneity across studies was quantified using the I^2 statistic, which estimates the proportion of total variability attributable to between-study differences. The Cochran's Q test was employed to formally assess heterogeneity. I^2 values were interpreted as follows: 0–30%, potentially negligible heterogeneity; 30–50%, moderate heterogeneity; 50–75%, substantial heterogeneity; and 75–100%, considerable heterogeneity.[29] To assess small-study effects and potential publication bias, contour-enhanced funnel plots depicting effect sizes against standard errors were generated.

Subgroup analyses were performed to assess AF recurrence according to ablation modality (radiofrequency vs. cryoballoon), arrhythmia subtype (paroxysmal vs. persistent), study design (prospective vs. retrospective), and ablation strategy—specifically, whether adjunctive lesion sets beyond pulmonary vein isolation were employed [PVI (+)] or not (PVI only). To ensure consistency with contemporary procedural standards, ablation strategies were classified in accordance with the 2024 European Heart Rhythm Association/Heart Rhythm Society/Asia Pacific Heart Rhythm Society/Latin American Heart Rhythm Society (EHRA/HRS/APHRS/LAHRS) expert consensus statement on catheter and surgical ablation of AF.[7] In this framework, adjunctive ablation was defined as the addition of one or more of the following lesion sets to PVI: cavotricuspid isthmus (CTI) ablation, linear lesions (e.g. roof or mitral isthmus lines), complex fractionated atrial electrogram ablation, posterior wall isolation, substrate modification targeting low-voltage areas, vein of Marshall ablation, non-pulmonary vein trigger ablation, or ganglionated plexi ablation. This classification reflects current expert consensus and was used to ensure methodological rigour and clinical relevance in our stratified analyses.[12]

Additionally, age-stratified analyses were performed for both the primary outcome and AF subtype, evaluating the differential impact of early vs. delayed ablation across age groups. Based on the age

distribution of study participants, four age strata were defined: (i) <55 years, (ii) 55–59 years, (iii) 60–64 years, and (iv) ≥65 years.

Sensitivity analysis

To ensure the robustness of the pooled estimates for the primary outcome, we conducted a series of leave-one-out meta-analyses, systematically omitting one study at a time to evaluate its influence on the overall effect size estimate and identify any disproportionately influential studies.

Furthermore, given that the conversion of binomial data to HRs led to the incorporation of unadjusted estimates into the pooled analysis, we conducted a sensitivity analysis restricted to studies reporting adjusted HRs that accounted for potential baseline confounders. This supplementary analysis aimed to evaluate the potential influence of disparities in baseline patient characteristics and strengthen the validity of the effect estimates by minimizing residual confounding.

Meta-regression analysis

To investigate potential sources of heterogeneity and effect modifiers across the included studies, univariate meta-regression analyses were performed using a frequentist framework, contingent upon the availability of a sufficient number of studies.[21] The meta-regression models incorporated the following covariates: difference in mean DAT between early and delayed ablation groups, follow-up duration, proportion of male participants, BMI, prevalence of baseline comorbidities (diabetes, hypertension, OSA, history of heart failure, stroke, or coronary artery disease), baseline LAD, LVEF, use of AADs or beta-blockers, CHA_2DS_2-VASc score, and year of studies' publication. These analyses aimed to identify variables influencing the observed effect estimates and to further elucidate potential determinants of variability in the meta-analytic findings.

Results

Study selection and characteristics

The PRISMA flow diagram, outlining the systematic database search and study selection process, is presented in Supplementary material online, *Figure S1*. Following the removal of duplicates, a total of 3891 records were initially retrieved and subjected to title and abstract screening. Of these, 3838 records were excluded based on relevance. The remaining 53 studies underwent a rigorous full-text evaluation, ultimately yielding 28 studies that met the predefined eligibility criteria.[30–57] A detailed account of excluded studies, along with the corresponding reasons for exclusion, is provided in Supplementary material online, *Table S4*.

The key characteristics of the included studies are summarized in *Table 1* and Supplementary material online, *Table S5*, while Supplementary material online, *Table S6* provides the list of variables used for confounder adjustment in the primary studies. Details of ablation strategies are provided in Supplementary material online, *Table S7*, while the follow-up monitoring methods used to ascertain AF recurrence are presented in Supplementary material online, *Table S8*. The definition of serious adverse events reported across included studies is detailed in Supplementary material online, *Table S9*. A total of 28 studies, encompassing 41 431 patients who underwent their first AF ablation, were analysed. The study population comprised 65% male participants, with mean ages ranging from 39 to 70 years. The median follow-up duration was 24 months (interquartile range: 12–36 months). Regarding the timing of ablation, the earliest recorded DAT in the early and delayed ablation groups was 2.4 months and 14 months, respectively, whereas the longest DAT extended to 9.6 months and 136 months, respectively. At the time of diagnosis, PAF and PsAF were reported in 53% and 45% of patients, respectively.

The ROBINS-I assessment indicated that most studies had a low risk of bias. Two studies[37,44] were rated as having serious concerns due to potential biases in outcome measurement and intervention classification (see Supplementary material online, *Table 10*).

Atrial fibrillation recurrence

A total of 26 studies, encompassing 39 903 patients with AF, evaluated the impact of DAT on AF recurrence, using a 1-year threshold to define early ablation. Over a median follow-up of 24 months, patients who underwent ablation within ≤1 year of diagnosis exhibited a significantly lower risk of AF recurrence compared to those with a DAT > 1 year [HR = 0.65, 95% CI = (0.59, 0.73), $P < 0.0001$; $I^2 = 59\%$, heterogeneity $P < 0.01$; *Figure 1*]. These findings remained consistent in a sensitivity analysis restricted to studies reporting adjusted HRs, demonstrating a comparable risk reduction [aHR = 0.65, 95% CI = (0.57, 0.74), $P < 0.0001$; $I^2 = 62\%$, heterogeneity $P < 0.01$; Supplementary material online, *Figure S2*].

Based on a subgroup analysis, the benefit of early ablation within the first year of AF diagnosis was consistent for both PAF [$n = 13{,}063$, HR = 0.72, 95% CI = (0.67, 0.77), $P < 0.0001$; $I^2 = 36\%$, heterogeneity $P = 0.11$] and PsAF [$n = 10{,}771$, HR = 0.70, 95% CI = (0.61, 0.81), $P < 0.0001$; $I^2 = 59\%$, heterogeneity $P < 0.01$; *Figure 2*]. Subgroup analysis comparing studies employing PVI alone vs. those utilizing adjunctive lesion sets demonstrated no significant differences ($P = 0.38$), with the association between early ablation and reduced AF recurrence remaining consistent across both subgroups (*Figure 3*). Furthermore, individuals who underwent radiofrequency ablation within ≤1 year of diagnosis experienced a greater reduction in AF recurrence risk compared to those who underwent cryoballoon ablation [aHR = 0.43, 95% CI = (0.43, 0.67), $P < 0.0001$; $I^2 = 59\%$, heterogeneity $P < 0.01$, vs. aHR = 0.74, 95% CI = (0.66, 0.82), $P < 0.0001$; $I^2 = 16\%$, heterogeneity $P = 0.31$; Supplementary material online, *Figure S3*]. This favourable association with early ablation was consistent across both prospective and retrospective studies, although significant heterogeneity persisted in the pooled analysis of prospective studies (see Supplementary material online, *Figure S4*).

The age-stratified analysis revealed that the benefit of early ablation was consistently observed across all age groups, with the greatest advantage observed in individuals younger than 55 years [HR = 0.49, 95% CI = (0.34, 0.71), $P < 0.0001$; $I^2 = 72\%$, heterogeneity $P = 0.01$; *Figure 3*]. However, the magnitude of the benefit was inversely associated with increasing age [≥55 and <60 years, HR = 0.53, 95% CI = (0.35, 0.79), $P < 0.0001$; $I^2 = 52\%$, heterogeneity $P = 0.03$; ≥60 and <65 years, HR = 0.66, 95% CI = (0.54, 0.81), $P < 0.0001$; $I^2 = 73\%$, heterogeneity $P < 0.01$; ≥65 years, HR = 0.65, 95% CI = (0.59, 0.71), $P < 0.0001$; $I^2 = 0\%$, heterogeneity $P = 0.91$; *Figure 4*). A similar age-dependent trend was observed within the PAF and PsAF subgroups (see Supplementary material online, *Figure S5*).

Individuals with a DAT of ≤3 years exhibited a significantly lower risk of AF recurrence compared to those with a DAT > 3 years [eight studies ($n = 17\,655$), HR = 0.70, 95% CI = (0.67, 0.74), $P < 0.0001$; $I^2 = 54\%$, heterogeneity $P = 0.03$; Supplementary material online, *Figure S6*). Moreover, the risk of AF recurrence increased by 10% for each additional year elapsed from AF diagnosis [HR = 1.10, 95% CI = (1.06, 1.15), $P < 0.001$; $I^2 = 82\%$, heterogeneity $P < 0.01$; Supplementary material online, *Figure S7*].

The contour-enhanced funnel plot, depicting the relationship between effect size and standard error for the assessment of small-study effects and publication bias, is presented in Supplementary material online, *Figure S8*. The sensitivity analysis, utilizing a leave-one-out approach, revealed no outliers or influential studies that significantly impacted the pooled effect estimates (see Supplementary material online, *Figure S9*).

Meta-regression analysis

The results of the meta-regression analyses are presented in *Figure 5*. These analyses showed that a larger gap in DAT between early and

Table 1 Characteristics of included studies

First author	Publication year	Study type	Follow-up in years, mean (SD)	Number of participants			DAT in months, mean (SD)		Age in years, mean (SD)		Males, *n* (%)		PAF (%)		PsAF (%)		LA diameter (mm)		HF at baseline (%)		AAD prior ablation (%)	
				Total	E	D	E	D	E	D	E	D	E	D	E	D	E	D	E	D	E	D
Bunch TJ[50]	2013	Observational cohort (retrospective)	3.2 (3.3)	684	303	381	N/R	N/R	63.1 (11.4)	63.4 (11.6)	62.4	60.4	57.1	58.2	26.8	28.8	N/R	N/R	21.7	36.2	41.2	42.1
Hussein AA[49]	2016	Observational cohort (prospective)	2	1241	382	859	N/R	N/R	60.9 (10.4)	61	78.3	18.6	0	0	100	100	N/R	N/R	N/R	N/R	N/R	N/R
De Greef Y[48]	2018	Observational cohort (retrospective)	3.7 (1.8)	1000	244	756	6 (3)	60.7 (48.5)	59 (10)	60 (10)	70	71.9	65.2	56.3	34.8	43.7	42 (7)	42.6 (7)	N/R	N/R	N/R	N/R
Lunati M[47]	2018	Observational cohort (prospective)	1.4 (0.7)	510	130	380	9 (4.5)	58.1 (50.6)	58.8 (11)	59.3 (10.5)	76.9	77.6	100	100	0	0	39.9 (6)	41.1 (5.7)	N/R	N/R	93.2	89.1
Bisbal F[46]	2019	Observational cohort (prospective)	1.2 (0.9)	309	51	258	8.7 (4.6)	52.2 (38.8)	55.8 (11.3)	56.8 (9.8)	62.5	72.6	62.5	68.9	37.5	31.1	39.9 (4.9)	41.7 (5.9)	N/R	N/R	77.1	
Kawaji T[45]	2019	Observational cohort (retrospective)	5 (2.5)	1206	389	817	3.1 (4.1)		64,3 (9,5)		71		70.7		29.3		40.9 (6.9)		8.5		39.1	
Chew DS[44]	2021	Observational cohort (retrospective)	1	11143	8118	3025	N/R	N/R	58.7 (8.2)	58.6 (8.2)	69	69.8	N/R	N/R	N/R	N/R	N/R	N/R	11.2	10.8	49.8	53.1
Solimene F[43]	2021	Observational cohort (prospective)	1 (0.35)	153	80	73	34.5 (49.4)		59 (10)		69.9		61.4		38.6		42 (7)		5.2		56.9	
Lycke M[41]	2021	Observational cohort (prospective)	1	325	149	176	19.7 (26.8)		62,5 (10,3)		30.9		100		0		41.3 (5.7)		2.2		N/R	
Takamiya T[40]	2021	Observational cohort (prospective)	2.2 (1.5)	502	408	94	6.7 (6.7)	60.7 (37.6)	65.3 (10.4)	61.9 (9.8)	78	87	0	0	100	100	42.5 (6.5)	43.4 (6.4)	22	18	N/R	N/R
Baysal E[39]	2022	Observational cohort (retrospective)	1	132	89	43	2.6 (2.3)	16.3 (8.1)	55.3 (13.6)	53.2 (16.1)	54	47	100	100	0	0	37.4 (5.3)	37.3 (6.9)	N/R	N/R	37	39
Robinson A[38]	2022	Observational cohort (retrospective)	1	182	66	116	5.3 (2.9)	42.5 (32.2)	62.2 (11.7)	66.8 (9.8)	70	60	77	71	23	29	42 (8)	42 (7)	N/R	N/R	N/R	N/R
Lador A[37]	2024	Observational cohort (retrospective)	2	601	347	254	N/R	N/R	69.8 (9.9)	68.5 (9)	56.7	57.9	28.2	29.9	17.6	8.7	N/R	N/R	72.7	69.2	N/R	N/R
Tóth P[36]	2024	Observational cohort (prospective)	3.5 (2.6)	227	101	126	N/R	N/R	64.7 (10.7)	63.9 (10.5)	76	86	50	58	50	42	57.1 (7.7)	57.9 (9.7)	100	100	N/R	N/R
Hein R[35]	2024	Observational cohort (retrospective)	1	1064	362	702	5.7 (4)	61.7 (48.7)	59.9 (10.6)	63.7 (10)	66.3	65.8	71	66.4	29	33.6	N/R	N/R	15.5	15.7	37.1	39.2
Nastasă A[34]	2024	Observational cohort (prospective)	3 (median)	107	22	85	4.4 (3.3)		54,3 (11,7)		57.5		66		34		N/R		28.3		N/R	
Segan L[33]	2024	Observational cohort (prospective)	1	210	72	138	5..7 (4.1)	47 (37.4)	61.8 (10)	61.4 (10.5)	73.6	86.2	0	0	100	100	N/R	N/R	100	100	51.4	55.1
Kwon CH[32]	2024	Observational cohort (retrospective)	1.75 (0.8)	2605	318	2287	N/R	N/R	60.9 (10)	61.8 (10)	72.6	77.3	40.9	57.5	59.1	42.5	42.3 (6.5)	44 (6.9)	16.7	24.7	N/R	N/R
Kim HJ[57]	2024	Observational cohort (prospective)	2.4 (1.9)	1038	336	700	28.9 (29.7)		61 (10,4)		79.8		0		100		43.6 (5.2)		25.1		100	
Farghaly AAA[56]	2024	Observational cohort (retrospective)	1.3 (0.7)	130	33	97	7.6 (1.3)	55 (5.2)	57.3 (12.8)	59.8 (9.9)	69.7	77.3	78.8	72.2	21.2	27.8	43.6 (5.2)	43.6 (5.2)	9.1	4.2	69.7	84.5
Ando M[55]	2024	Observational cohort (prospective)	1.95 (1.5)	543	278	265	3.6 (1.8)	28.2 (26.8)	70 (8.8)	68.5 (11.1)	55	60	73	71	27	29	43.6 (5.2)	43.6 (5.2)	100	100	29	55
Crowley R[54]	2024	Observational cohort (prospective)	1	334	84	250	6.6 (5.1)	61.7 (58.9)	64.5 (9.6)	65 (9.6)	75	77.6	0	0	100	100	43.6 (5.2)	43.6 (5.2)	47.6	41.2	86.9	92.8
Erhard N[53]	2024	Observational cohort (retrospective)	1.4 (2.3)	101	51	50	6 (8.3)	100 (173)	47.5 (13)	43.7 (22.1)	90.2	72	0	0	100	100	43.6 (5.2)	43.6 (5.2)	N/R	N/R	N/R	N/R
Tønnesen J[52]	2024	Observational cohort (retrospective)	2.7 (2.3)	7705	2588	5177	5.5 (3.4)	66 (52.8)	60.6 (11.1)	62.8 (9.8)	72.1	67.4	61.5	49.7	38.5	50.3	43.6 (5.2)	43.6 (5.2)	16.7	17	35.6	41.4
Zhou L[51]	2024	Observational cohort (retrospective)	3.3 (2.6)	1694	544	1150	2.4	105	38.6 (5.6)	38.1 (6)	80.9	84	66.7	55.2	33.3	44.8	43.6 (5.2)	43.6 (5.2)	5.2	3.9	41	51.6
Lawin D[30]	2025	Observational cohort (prospective)	2	3447	1573	1874	4.8 (3.6)	63.6 (61.2)	62 (12)	61 (11)	64.2	63.8	71.4	75	58.5	25	43.6 (5.2)	43.6 (5.2)	36.5	34.6	N/R	N/R
Stabile G[42]	2024	Observational cohort (prospective)	3	3143	N/R	N/R	50.4 (58.6)		60,5 (10,6)		71.6		78.8		21.2		41.3 (7.9)		4		N/R	
Huang W[31]	2024	Observational cohort (prospective)	2.3 (1.55)	1095	507	588	4 (4.6)	57.8 (53)	4 (4.6)	57.8 (53)	50.9	50.2	55.4	56.3	44.6	43.7	41 (5)	42 (6)	16	18.9	N/R	N/R
Lawin D[30]	2025	Observational cohort (prospective)	2	3447	1573	1874	4.8 (3.6)	63.6 (61.2)	62 (12)	61 (11)	64.2	63.8	71.4	75	58.5	25	43.6 (5.2)	43.6 (5.2)	36.5	34.6	N/R	N/R

All characteristics are presented using a DAT ≤ 1 year as the cut-off to define the early ablation group, except for the studies by Kawaji and Takamiya *et al.*, where a DAT ≤ 3 years is used instead due to the absence of a 1-year cut-off in their data.

AAD, antiarrhythmic drug; AF, atrial fibrillation; D, delayed ablation group; DAT, diagnosis-to-ablation time; E, early ablation group; HF, heart failure; LA, left atrial; N/R, not reported SD, standard deviation.

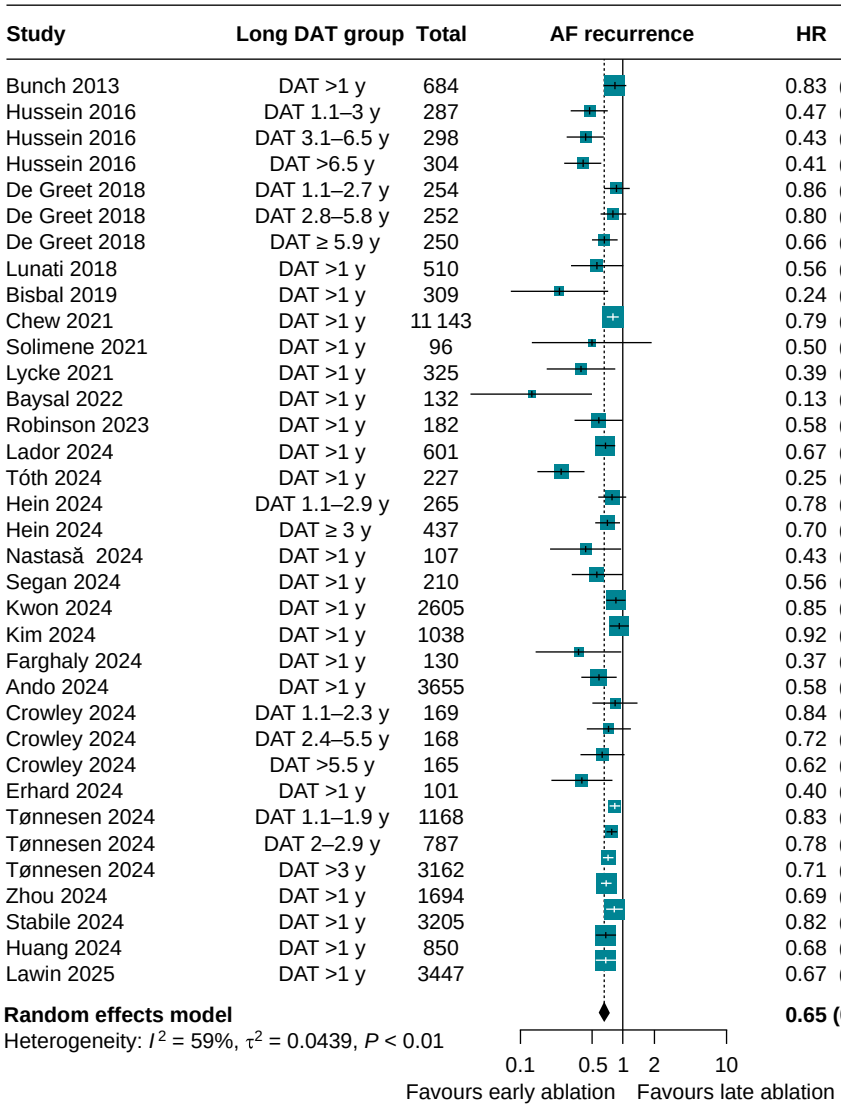


Figure 1 Forest plots depicting the impact of DAT on AF recurrence, comparing individuals with a DAT of ≤1 year vs. >1 year. AF, atrial fibrillation; CI, confidence interval; DAT, diagnosis-to-ablation time; HR, hazard ratio.

delayed ablation groups was significantly associated with a lower risk of AF recurrence in the early ablation group. Additionally, a higher CHA_2DS_2-VASc score correlated with a reduced risk of AF recurrence among patients undergoing early AF ablation, compared to delayed ablation. Studies with an increased prevalence of heart failure among participants reported a significantly lower risk of AF recurrence in the early ablation group compared to the delayed ablation group. Baseline left LVEF emerged as a significant moderator of the pooled risk, with the benefit from early ablation procedure being more pronounced in patients with lower LVEF. No significant effect modification was observed for the other covariates (see Supplementary material online, *Figures S10–S13*). Moreover, most of the meta-regression analyses did not explain a substantial proportion of heterogeneity, as indicated by the R^2 values.

Repeat ablation and new cardioversion

The risk of repeat ablation was significantly lower in individuals with a DAT duration of ≤1 year compared to those with a DAT duration of >1 year [nine studies (n = 6865), risk ratio (RR) = 0.70, 95% CI = (0.51, 0.95), P < 0.0001; I^2 = 59%, heterogeneity P = 0.01; *Figure 6A*]. Similarly, the risk of new cardioversion was significantly lower in the ≤1-year DAT group than in the >1-year DAT group [six studies (n = 5761), RR = 0.60, 95% CI = (0.48, 0.74), P < 0.0001; I^2 = 0%, heterogeneity P = 0.47; *Figure 6B*).

Cardiovascular hospitalization and mortality

Diagnosis-to-ablation time of ≤1 year was significantly associated with a reduced risk of cardiovascular hospitalization [eight studies (n = 8373), RR = 0.74, 95% CI = (0.63, 0.88), P < 0.0001; I^2 = 44%, heterogeneity P = 0.08; *Figure 6C*). However, no significant differences were observed in the risk of cardiovascular or all-cause mortality when using a DAT threshold of 1 year (*Figures 6D and E*).

Serious periprocedural adverse events

The risk of serious periprocedural adverse events did not differ significantly between patients with DAT duration of ≤1 year and >1 year

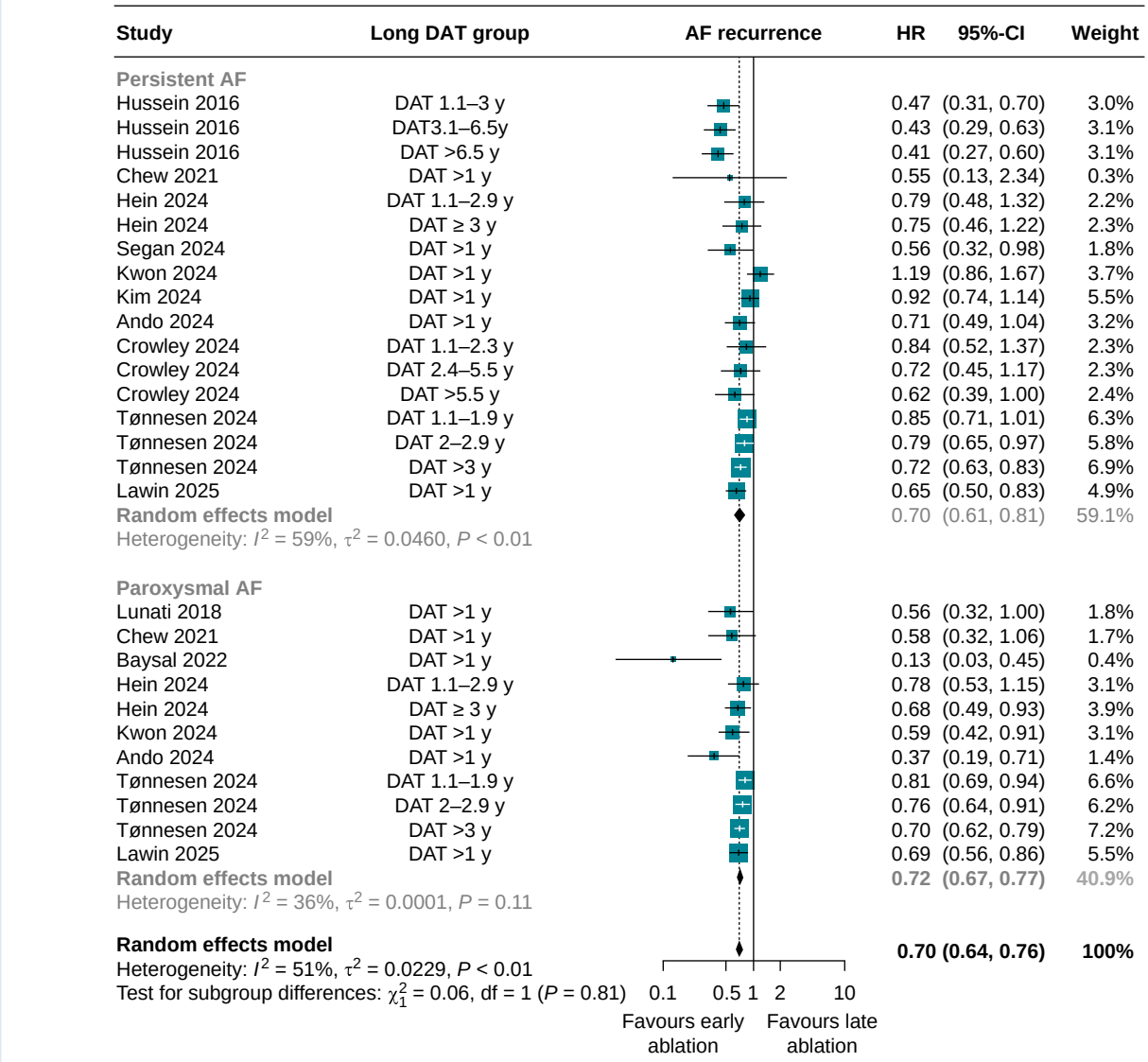


Figure 2 Forest plots illustrating the impact of DAT on AF recurrence, stratified by AF type, comparing individuals with a DAT of ≤1 year vs. >1 year. AF, atrial fibrillation; CI, confidence interval; DAT, diagnosis-to-ablation time; HR, hazard ratio.

[RR = 0.76, 95% CI = (0.54, 1.05), P < 0.0001; I^2 = 6%, heterogeneity P = 0.38; Supplementary material online, Figure 14].

Use of antiarrhythmic medication prior to index ablation

Patients with a DAT duration of ≤1 year had significantly lower odds of receiving AADs prior to the ablation procedure compared to those with a longer DAT [odds ratio OR = 0.75, 95% CI = (0.60, 0.93), P < 0.001; I^2 = 75%, heterogeneity P < 0.01; *Figure 7*].

Discussion

Summary of main findings

This comprehensive meta-analysis assessed the relationship between DAT and age-stratified AF recurrence and clinical outcomes in 41 431 patients with AF. The findings demonstrated that patients who underwent ablation within 1 year of diagnosis had a 35% lower risk of AF recurrence compared to those with a DAT exceeding 1 year. This benefit was observed in both PAF and PsAF. Notably, patients younger than 55 years derived the greatest reduction in AF recurrence risk when ablated within 1 year of diagnosis compared to those undergoing ablation beyond this timeframe. Although the advantage of early ablation remained significant across all age groups, its impact progressively declined with advancing age. Moreover, the benefit of early ablation was more pronounced in populations with higher CHA_2DS_2-VASc scores, greater heart failure prevalence, and lower mean LVEF. Patients with a DAT of ≤1 year were significantly less likely to have received medical rhythm control therapy prior to ablation compared to those with a longer DAT.

Atrial fibrillation and atrial remodelling

Early investigations established that AF contributes to progressive atrial remodelling, encompassing both electrical and structural alterations.[10,58] Initially, the concept of 'AF begets AF' was attributed to acute

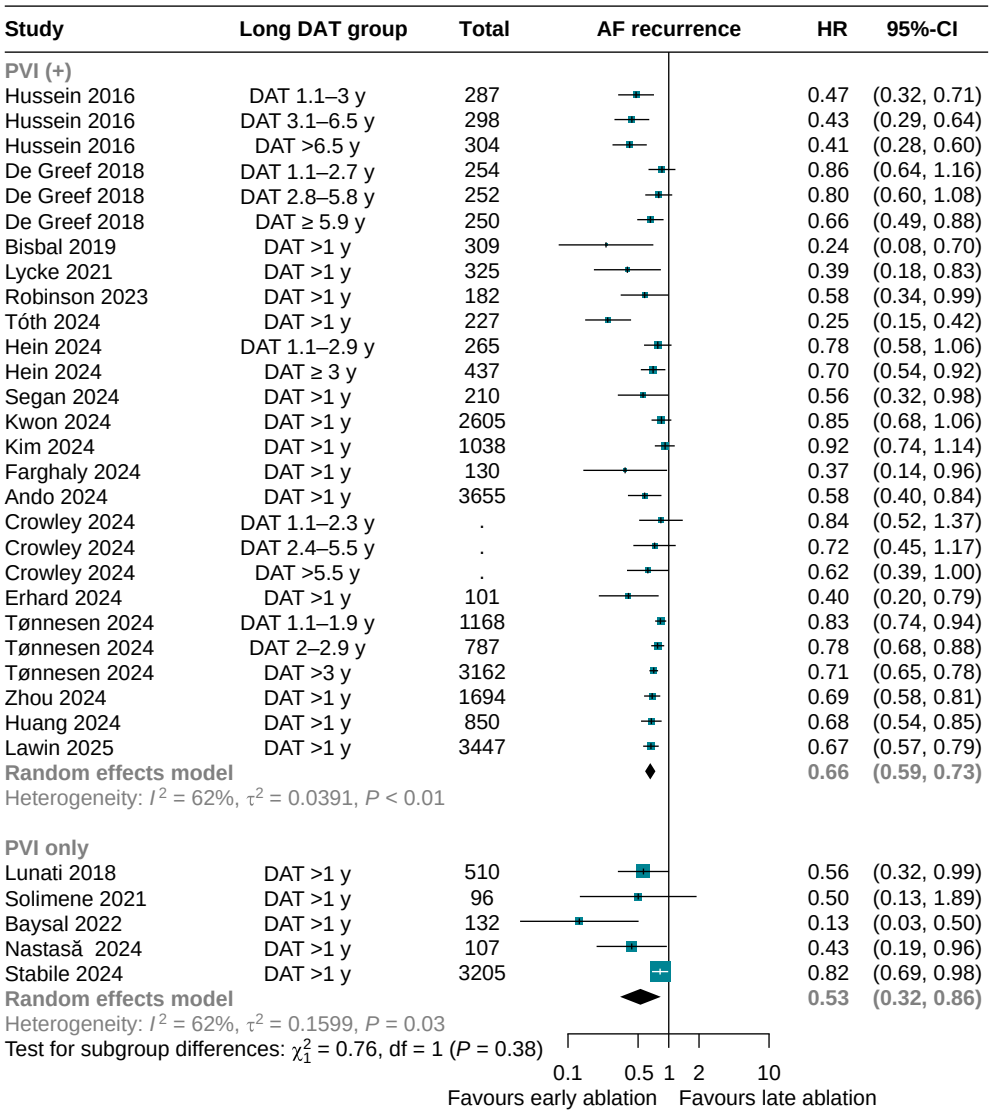


Figure 3 Forest plots depicting the impact of DAT on AF recurrence, stratified by ablation strategy—whether adjunctive ablation beyond PVI was performed [PVI (+)] or not (PVI only)—comparing patients with DAT ≤1 year vs. >1 year. AF, atrial fibrillation; CI, confidence interval; DAT, diagnosis-to-ablation time; HR, hazard ratio.

changes in atrial refractoriness; however, subsequent research revealed that prolonged AF episodes lead to significant structural remodelling.[58] Further studies demonstrated that atrial remodelling can also occur independently of AF due to underlying conditions such as heart failure, hypertension, and other pathological stimuli, leading to the characterization of this process as a distinct form of remodelling.[59,60]

The relationship between modifiable risk factors and the development of AF has been recognized for decades.[61–65] More recently, human mapping studies have provided mechanistic insights, demonstrating a dose-dependent effect of these risk factors on atrial substrate remodelling.[66–69] Specifically, the presence of conduction slowing, low-voltage areas, atrial scarring, and complex atrial electrograms has been associated with risk factors such as obesity, OSA, hypertension, heart failure, excessive alcohol consumption, and advancing age. In parallel, the extent of atrial remodelling has been linked to clinical risk stratification models, with scoring systems such as APPLE, DR-FLASH, and MB-LATER incorporating these risk factors to predict disease progression.[70,71]

Human studies have demonstrated that patients with PsAF exhibit more advanced electrical and structural atrial remodelling compared to those with PAF, suggesting that AF-related remodelling progresses over time and is influenced by AF burden.[72,73] However, the rate of the remodelling process and the AF burden threshold required to influence its progression remain incompletely understood, largely due to limited available data. The findings of our study, which demonstrate a marked decline in ablation efficacy beyond the first year following AF diagnosis, suggest that AF-driven remodelling advances rapidly within this critical window. Furthermore, these results imply that a 1-year duration may be sufficient for remodelling to reach a stage where it becomes extensive and potentially irreversible. While this phenomenon may be plausible in cases of high-burden PAF and PsAF, it is less likely that infrequent and relatively brief AF episodes alone account for the

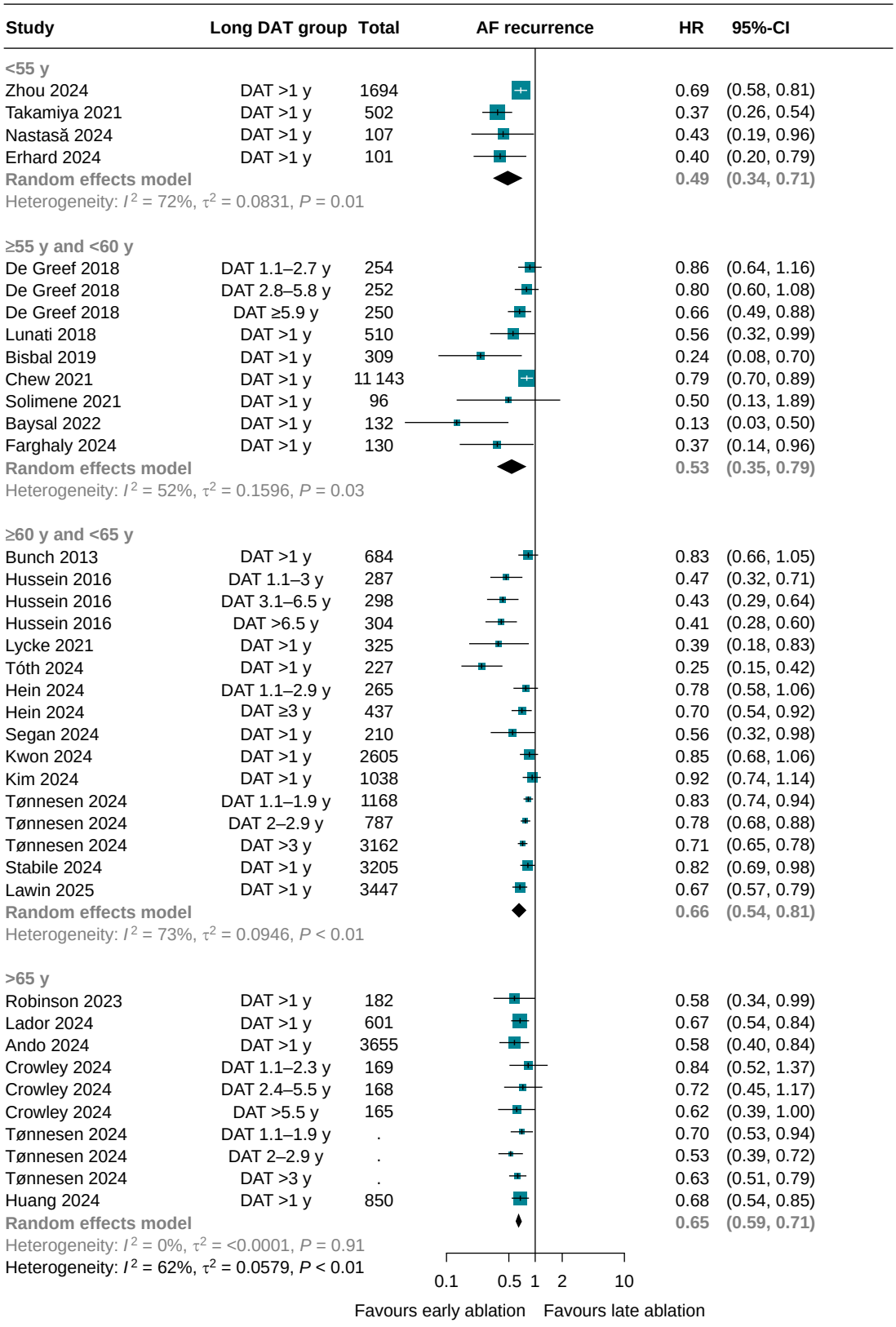


Figure 4 Forest plots illustrating the impact of DAT on AF recurrence, stratified by age, comparing individuals with a DAT of ≤1 year vs. >1 year. AF, atrial fibrillation; CI, confidence interval; DAT, diagnosis-to-ablation time; HR, hazard ratio.

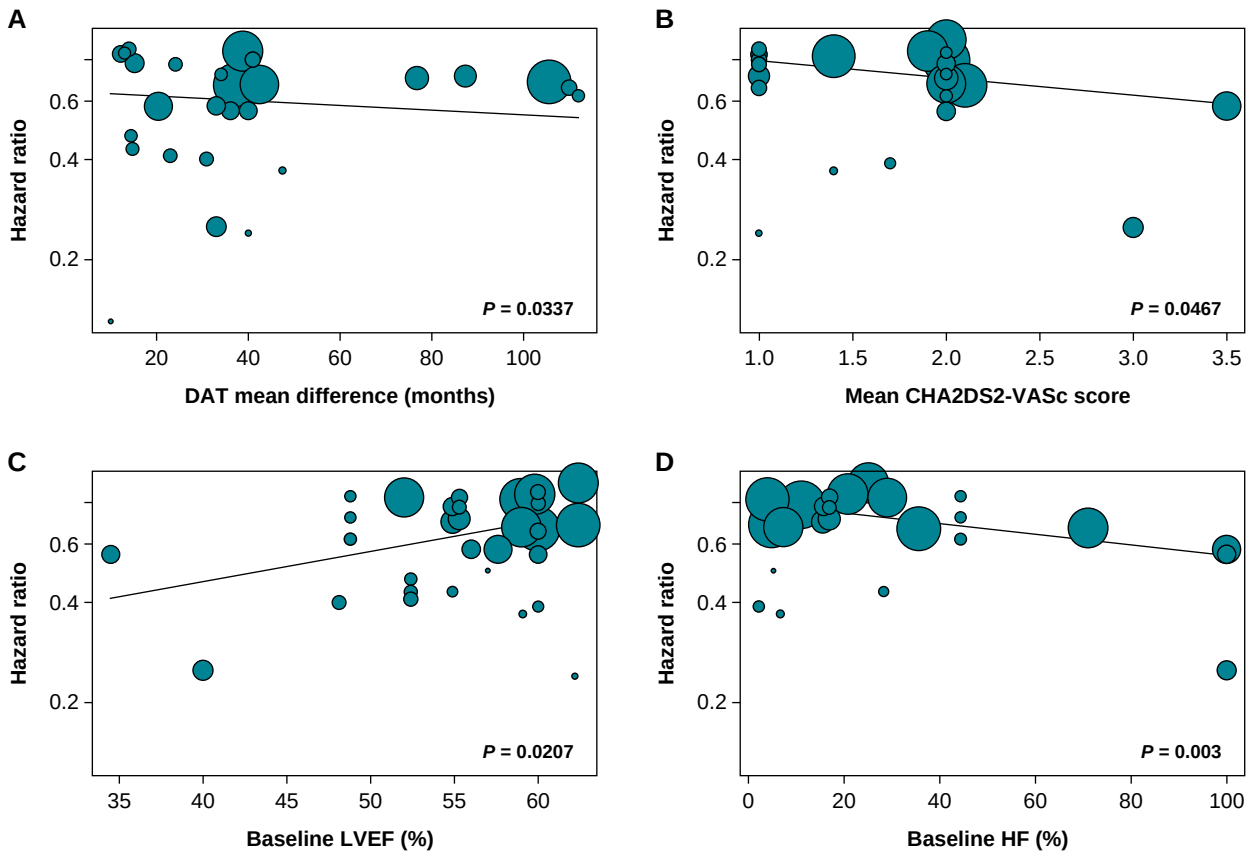


Figure 5 Bubble plots from the meta-regression analyses illustrating the association between DAT (≤1 year vs. >1 year) and AF recurrence, incorporating the following covariates in the meta-analytic models: mean difference in DAT between early and delayed ablation (*A*), mean CHA_2DS_2-VASc score (*B*), baseline LVEF (*C*), and prevalence of heart failure at baseline (*D*). DAT, diagnosis-to-ablation time; HF, heart failure; LVEF, left ventricular ejection fraction.

progressive remodelling that occurs in the intervals between episodes over weeks or months. Supporting this concept, a study involving a cohort of patients with high-burden PAF and continuous rhythm monitoring via implanted loop recorders assessed atrial remodelling through serial echocardiographic evaluations and P-wave duration measurements at 4-month intervals over a 12-month period.[74] Notably, only patients with an AF burden exceeding 10% exhibited a progressive decline in left atrial strain, indicating worsening atrial contractile function, alongside an increase in P-wave duration, reflective of atrial conduction slowing.[74] In contrast, individuals with an AF burden below this threshold showed no significant changes in these parameters over the same period.[74] Moreover, the study demonstrated that successful catheter ablation can halt and even reverse aspects of atrial remodelling over a 12-month follow-up, underscoring the potential benefits of early intervention in mitigating disease progression.[74]

Implications for clinical practice

In specific clinical scenarios, there is a broad consensus on the necessity of timely ablation. According to the 2024 ESC guidelines for AF management, this includes symptomatic PAF or PsAF, either after pharmacologic therapy failure or as a first-line intervention for PAF.[8] Similarly, both indications were assigned a 'To Do' recommendation in the most recent international consensus statement,[7] based on data from multiple RCTs.[15,16,75–77] The 2023 ACC/AHA/ACCP/HRS AF guidelines endorsed this recommendation with a Class I, Level of Evidence A designation for two comparable statements.[78] However, this endorsement was accompanied by the qualification that early ablation is generally most appropriate for younger patients with minimal comorbidities.[78]

Several key observations arise from our analysis. First, timely ablation is recommended for both PAF and PsAF in cases where pharmacologic therapy has failed. Notably, our findings suggest that patients who underwent delayed ablation had higher odds of prior AAD use. This may indicate that delaying ablation in favour of AAD therapy as a first-line approach—despite its proven inferiority to ablation—often results in later intervention, typically more than a year after diagnosis and at an older age, ultimately leading to less favourable outcomes compared to earlier intervention in younger patients.

Second, while first-line ablation is recommended for PAF, its role in PsAF is less emphasized. The latest 2024 ESC guidelines for AF management highlight that although multiple RCTs support catheter ablation as a first-line approach for rhythm control in PAF, its superiority over drug therapy as a first-line treatment in PsAF remains uncertain.[8] However, our analysis did not reveal significant differences in AF recurrence between early-treated PAF and PsAF patients. Subgroup analysis showed a comparable 30% reduction in AF recurrence in both groups, suggesting that the higher AF burden in PsAF may contribute to continuous atrial remodelling and could warrant earlier intervention to improve outcomes.

Third, as AF ablation currently holds a Class I recommendation for patients with concurrent AF and HFrEF, our findings further indicate

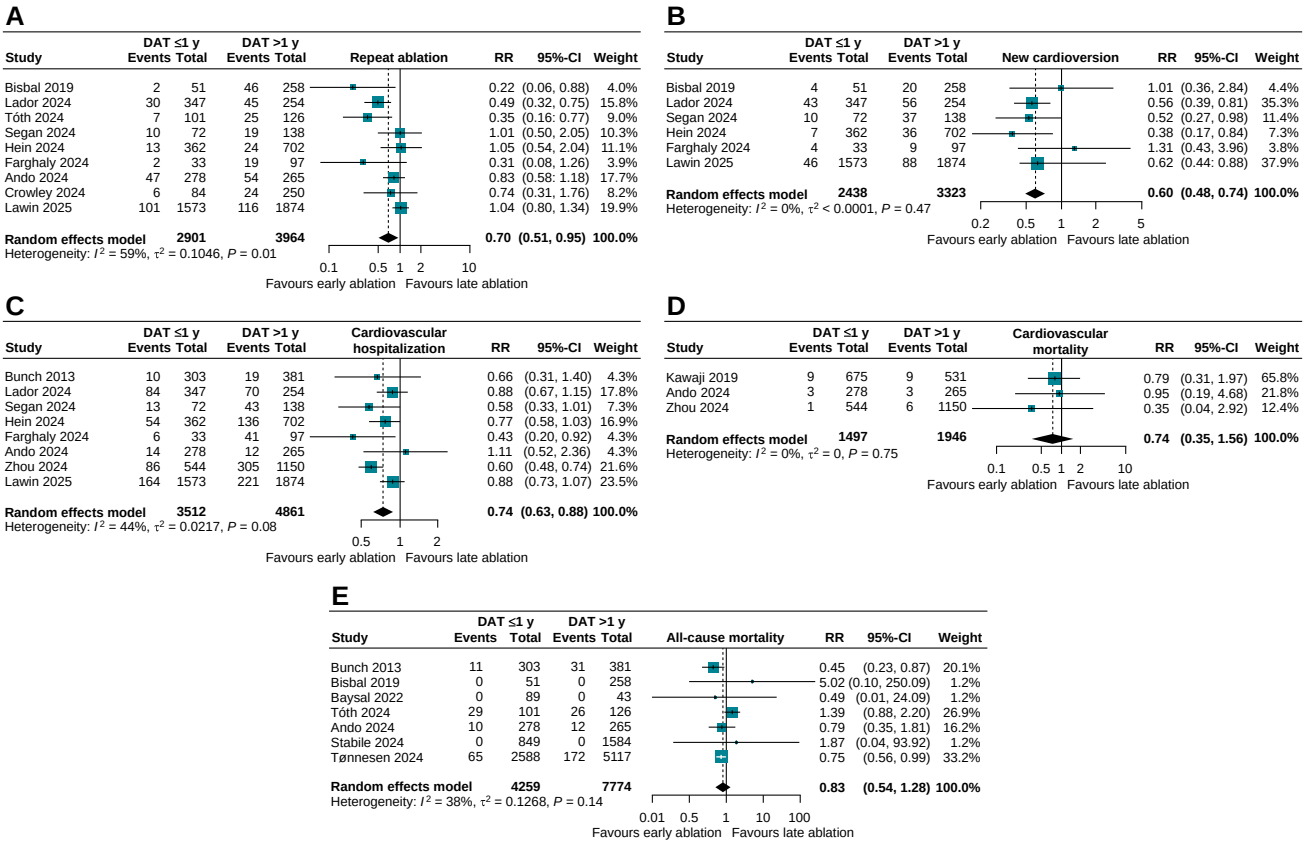


Figure 6 Forest plots illustrating the impact of DAT on repeat ablation (*A*), new cardioversion (*B*), cardiovascular hospitalization (*C*), cardiovascular mortality (*D*), and all-cause mortality (*E*) in individuals with a DAT of ≤1 year vs. >1 year. CI, confidence interval; DAT, diagnosis-to-ablation time; RR, risk ratio.

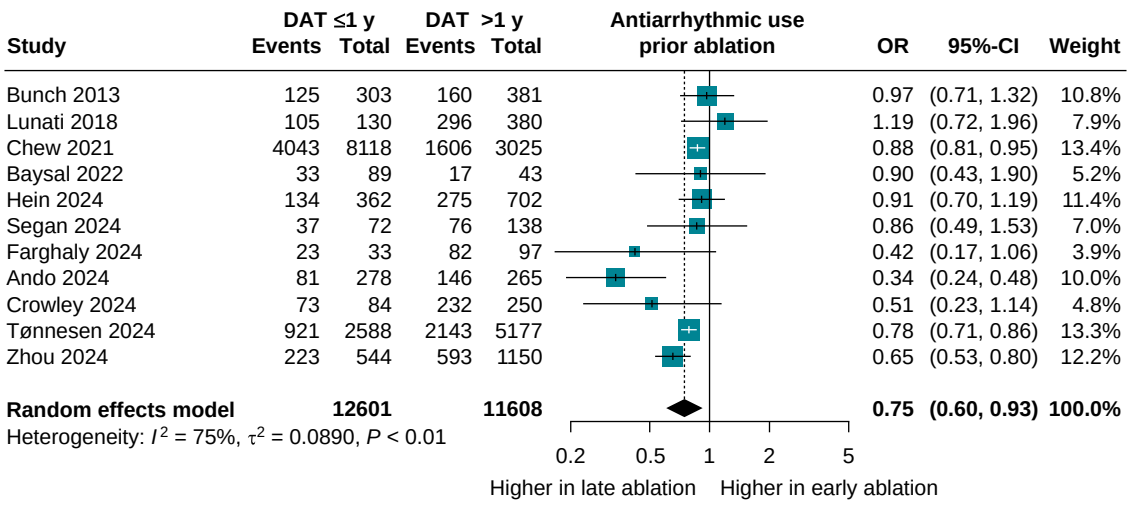


Figure 7 Forest plot illustrating the odds of AAD use prior AF ablation in individuals with a DAT of ≤1 year vs. >1 year. CI, confidence interval; DAT, diagnosis-to-ablation time; OR, odds ratio.

that this intervention may yield optimal outcomes when performed within one year of AF diagnosis. This is supported by our meta-regression analysis, which identified LVEF as a significant effect modifier of AF recurrence. Specifically, studies involving patients with lower mean LVEF reported a greater benefit from early ablation compared to those with higher mean LVEF, highlighting the potential advantage of timely intervention in this patient population.

Fourth, our findings indicate that studies with higher CHA_2DS_2-VASc scores reported a lower risk of AF recurrence in patients who underwent ablation within 1 year of diagnosis. Given that this scoring system incorporates well-established risk factors and comorbidities associated with AF progression, these results partially challenge the ACC/AHA/ACCP/HRS guideline's endorsement that early ablation is most beneficial for younger patients with minimal comorbidities. Instead, our findings suggest that individuals with a higher comorbidity burden may derive an even greater benefit from early intervention.

Strengths and limitations

Despite the rigorous execution of our study, several limitations merit acknowledgment. First, our analysis was conducted at the trial level without access to individual-level data. Second, as all included studies were observational cohorts, inherent variations in baseline patient characteristics, potential selection biases, and moderate heterogeneity were present; however, meta-regression analyses indicated that key clinical characteristics and comorbidities did not significantly influence the pooled effect estimates. Third, the age-stratified analysis of AF recurrence in PAF lacked relevant data for individuals under 55 and over 65 years. Fourth, the limited availability of data regarding AF burden, patient-reported outcomes, and quality-of-life measures precluded further meaningful analyses, and thus, these important endpoints remain to be addressed in future research. Fifth, a part of the moderate heterogeneity observed may stem from variations in the duration of undiagnosed AF prior to clinical detection—an aspect that could not be accounted for. Nevertheless, this limitation reflects the reality of clinical practice, where the precise onset of AF is often indeterminate. Sixth, as with all meta-analyses, our findings are potentially subject to publication bias, as studies with statistically significant or positive outcomes are more likely to be published and included. Furthermore, while some meta-regression findings reached statistical significance, they should be interpreted cautiously given the potential influence of outliers; these analyses are exploratory in nature and intended to generate hypotheses for future prospective research. Finally, no studies employing pulsed field ablation (PFA) technology were available, leaving the generalizability of our associations to PFA uncertain.

Conclusions

This meta-analysis indicates that patients with a DAT interval of ≤1 year undergoing catheter ablation may experience a significantly reduced risk of AF recurrence—across all AF types—as well as lower rates of repeat ablation, new cardioversion, and cardiovascular hospitalization, compared to those with a longer DAT. Notably, the benefits of early ablation appear consistent across age groups and show an inverse correlation with age, with younger individuals exhibiting a lower risk of AF recurrence than older patients. Additionally, patients with higher CHA_2DS_2-VASc scores seem to benefit more from undergoing early ablation procedure. Further long-term research, particularly RCTs with stratified patient populations, is essential to elucidate the implications of our findings and potentially refine clinical guidelines with more robust recommendations for the optimal timing of AF ablation procedure.

Supplementary material

Supplementary material is available at *Europace* online.

Authors' Contributions

P.K.: conceptualization, methodology, investigation, formal analysis, data curation, visualization, project administration, writing—original draft, and writing—review & editing. S.T.: conceptualization, methodology, investigation, writing—review & editing, validation, and supervision. K.P.: Writing—review & editing. A.S.: writing—review & editing. P.T.: writing—review & editing. N.M.: writing—review & editing. D.T.: writing—review & editing. M.E.: writing—review & editing. A.P.A.: writing—review & editing. N.F.: conceptualization, methodology, investigation, writing—review & editing, validation, and supervision. All authors read and approved the final manuscript.

Protocol

The study protocol was prospectively registered in OSF (https://osf.io/bmjyc/).

Conflict of interest: none declared.

Data availability

The data underlying this article will be shared on reasonable request to the corresponding author. The items outlined in the PRISMA 2020 checklist and their corresponding locations within the manuscript are presented in Supplementary material online, *Table 11*.

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