Repurposing SGLT2 Inhibitors for Rhythm Control After AF Ablation: Evidence from a Meta-Analysis

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Background

- AF is the most common sustained arrhythmia and a major contributor to morbidity, mortality and healthcare burden [1].

- Rhythm control is important for these patients however, previous research has indicated that antiarrhythmic drug therapy for the maintenance of sinus rhythm in AF patients is limited by the toxic side effects [1].

- Catheter ablation has become the first-line option for symptomatic AF patients who do not respond to drug therapy [2].

- Catheter ablation improves rhythm control but up to 40% of patients still experience AF recurrence within one year [2].

- Sodium-glucose cotransporter-2 inhibitors (SGLT2i), originally introduced for glucose lowering, have demonstrated additional cardiovascular benefits including natriuresis, anti-inflammatory and antifibrotic effects and improved myocardial metabolism [3,4].

Objectives

- Emerging evidence suggests these SGLT2i agents may also reduce AF recurrence after ablation, although the strength of this association and consistency across patient subgroups remain uncertain.

- To address this gap, we performed a systematic review and meta-analysis to determine whether SGLT2 inhibitor therapy is linked to a lower risk of post-ablation AF recurrence.

Methods

- The literature search, inclusion criteria, data extraction, and analyses in this study were conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.

- Electronic databases including PubMed, Embase and Cochrane Library were searched from inception to August 2025.

- The primary outcome was AF recurrence at the longest follow-up. When reported, both hazard ratios (HRs) and risk/odds ratios (RRs/ORs) were extracted. Effect estimates were pooled using a random-effects model to account for clinical and methodological heterogeneity across studies. For studies reporting raw event counts, risk ratios were calculated directly. For studies providing HRs or adjusted HRs, the generic inverse-variance method was applied.

- Heterogeneity was assessed with I^2 and Tau^2 where where I^2 >50% indicated a high heterogeneity between studies while I^2 <50% considered small or non-significant heterogeneity between studies.

Study Selection

- Inclusion Criteria:
    1. Randomized controlled trials or observational cohort studies
    2. Comparing SGLT2 inhibitor therapy vs control (no SGLT2i)
    3. Conducted in adult patients (≥18 years)
    4. Undergoing catheter ablation for atrial fibrillation
    5. Including paroxysmal, persistent, or long-standing persistent AF
    6. AF recurrence was defined as an episode of atrial tachyarrhythmia lasting ≥30 seconds occurring after the 3-month post-ablation period.
- Exclusion Criteria:
    1. No comparator group.
    2. No post-ablation rhythm outcomes.
    3. Pediatric populations.
    4. Non-ablation AF management studies.
    5. Reviews, abstracts, case reports or non-extractable data.

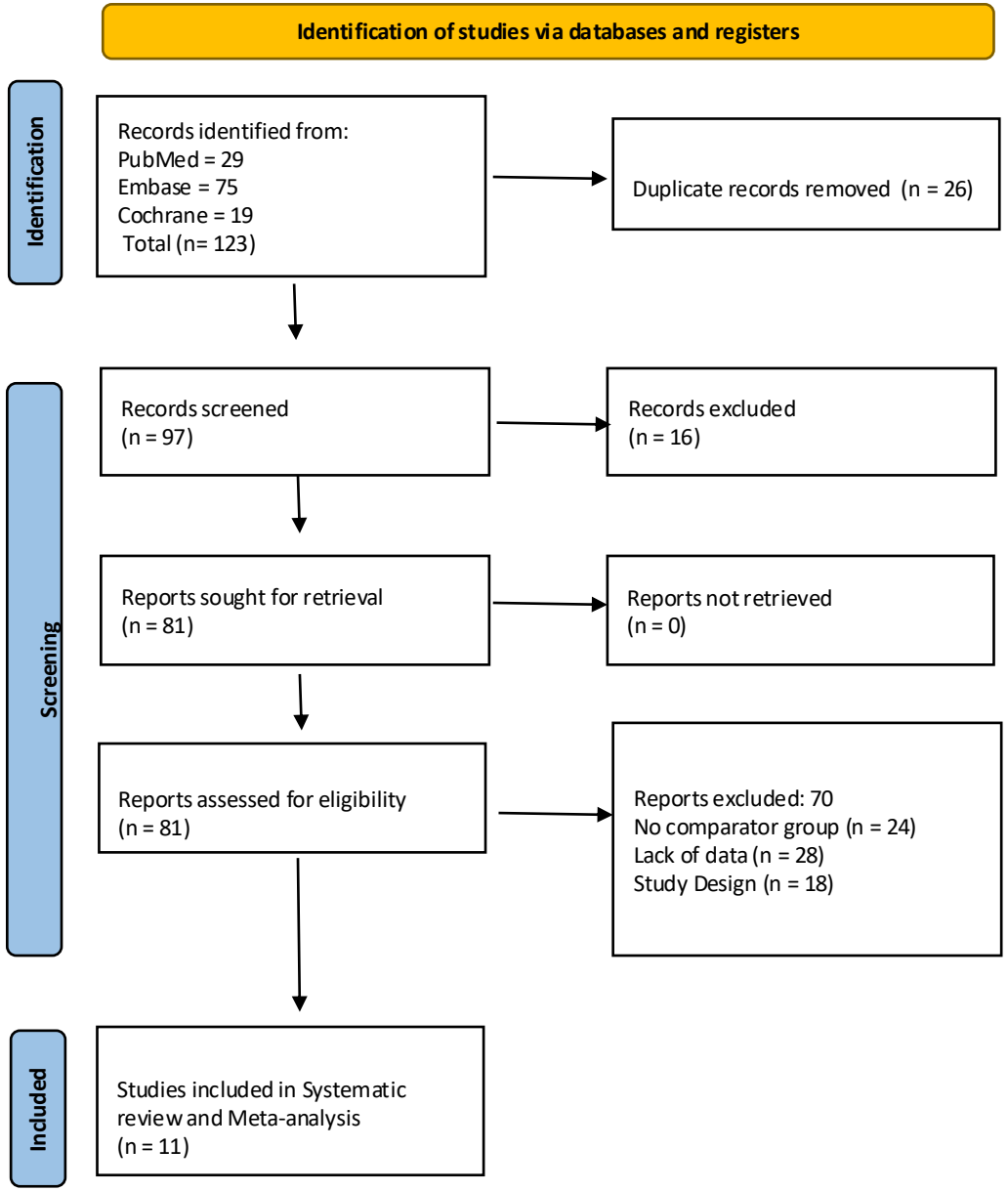


Figure 1. PRISMA Flow Chart

STUDY	STUDY DESIGN	TYPE OF SGLT2i	SAMPLE SIZE SGLT2i	AGE (MEAN ± SD) SGLT2i	FEMALE % SGLT2i	HEART FAILURE % SGLT2i	DIABETES % SGLT2i	FOLLOW-UP (MONTHS)
HARADA 2024 [5]	RCT	Empagliflozin Dapagliflozin	51	72.0 ± 8.3	35.2	100	0	12
XU 2025 [6]	Retrospective cohort	Empagliflozin Dapagliflozin	573	63.6 ± 9.7	28	48.3	90	20
CHEN 2025 [3]	Retrospective cohort	Empagliflozin Dapagliflozin	209	60.8 ± 9.9	40.7	18.7	17.2	12
CETIN 2025 [7]	Retrospective cohort	Empagliflozin Dapagliflozin	71	65.1 ± 7.9	39.4	NR	36.6	11.5
KHAN 2025 [2]	Retrospective cohort	Canagliflozin Dapagliflozin	6180	68.7 ± 8.3	29	60.9	100	12
NOH 2024 [8]	Retrospective cohort	Empagliflozin Dapagliflozin	73	72.19 ± 5.45	73.5	NR	38	18
LUO F 2024 [9]	Retrospective cohort	Dapagliflozin	79	63.7 ± 10	41.1	NR	100	15.5
ABU QAOUD 2023 [1]	Retrospective cohort	-	2225	65 ± 9	26	60	100	12
LIU 2023 [10]	Retrospective cohort	Empagliflozin Canagliflozin	45	60.1 ± 10.6	22	26	100	33.7
ZHAO 2023 [11]	Retrospective cohort	Dapagliflozin Canagliflozin Dapagliflozin Tofogliflozin	138	63.9 ± 8.7	29	21	100	18
KISHIMA 2022 [12]	RCT	Empagliflozin Tofogliflozin	38	70.3 ± 8.6	32	27	100	12

Table 1. Baseline Characteristics of the included studies.

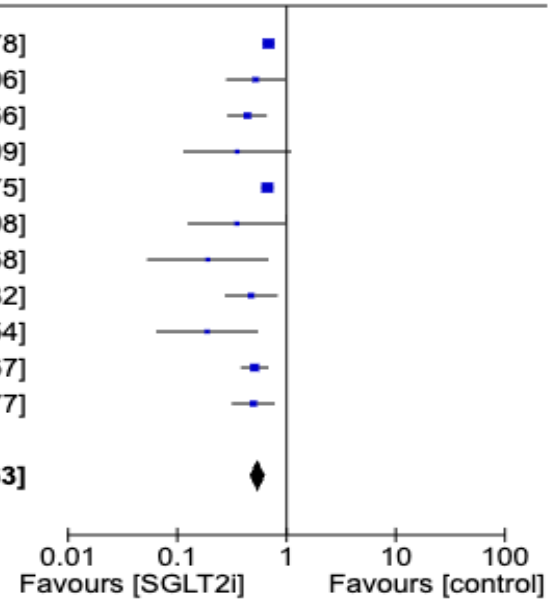
Results

- 11 studies were included, comprising 19,059 patients.
- 9,674 patients received an SGLT2 inhibitor.
- Mean age across studies ranged from 60 to 72 years.
- Women accounted for 25% to 74% of participants.
- Diabetes prevalence varied between 0% and 68%.
- Median follow-up duration across studies was approximately 11–12 months.

Results

Study or Subgroup	SGLT2i Events	SGLT2i Total	Control Events	Control Total	Weight	Odds ratio M-H, Random, 95% CI
Abu Qaoud	619	2225	802	2225	22.9%	0.68 [0.60 , 0.78]
Cetin	18	71	69	175	5.5%	0.52 [0.28 , 0.96]
Chen	40	209	131	373	10.0%	0.44 [0.29 , 0.66]
Harada	5	51	12	51	1.9%	0.35 [0.11 , 1.09]
Khan	545	6180	782	6180	23.5%	0.67 [0.59 , 0.75]
Kishima	9	38	15	32	2.3%	0.35 [0.13 , 0.98]
Liu	3	45	21	77	1.5%	0.19 [0.05 , 0.68]
Luo	22	79	111	247	6.5%	0.47 [0.27 , 0.82]
Noh	5	65	20	65	2.2%	0.19 [0.07 , 0.54]
Xu	100	573	168	573	14.8%	0.51 [0.38 , 0.67]
Zhao	33	138	150	387	8.9%	0.50 [0.32 , 0.77]
Total (Wald[a])		**9674**		**10385**	**100.0%**	**0.54 [0.46 , 0.63]**
Total events:	1399		2281			

Test for overall effect: Z = 7.46 (P < 0.00001)



Heterogeneity: Tau² (DL[b], 95% CI) = 0.03 [0.00 , 0.37]; Chi² = 21.14, df = 10 (P = 0.02); I² = 53%

Footnotes

[a]CI calculated by Wald-type method.

[b]Tau² calculated by DerSimonian and Laird method.

Figure 2. Forest plot of AF recurrence rate between SGTL2i and control group. SGLT2 inhibitors had 46% lower odds of AF recurrence compared to controls.

Results

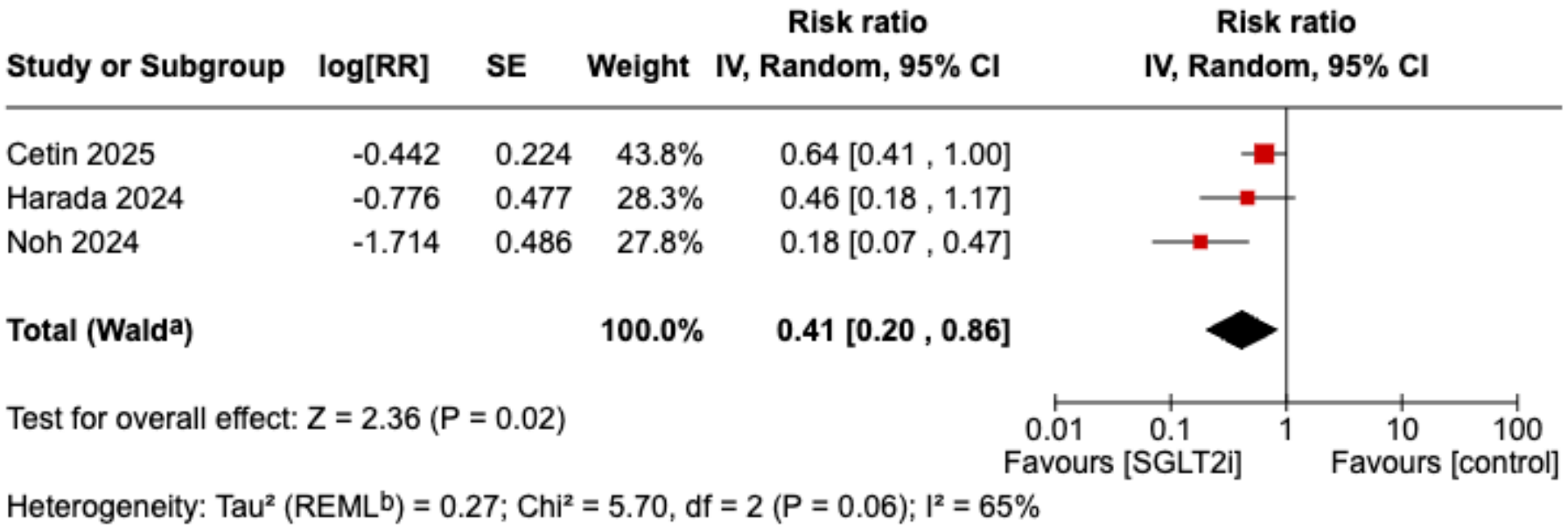
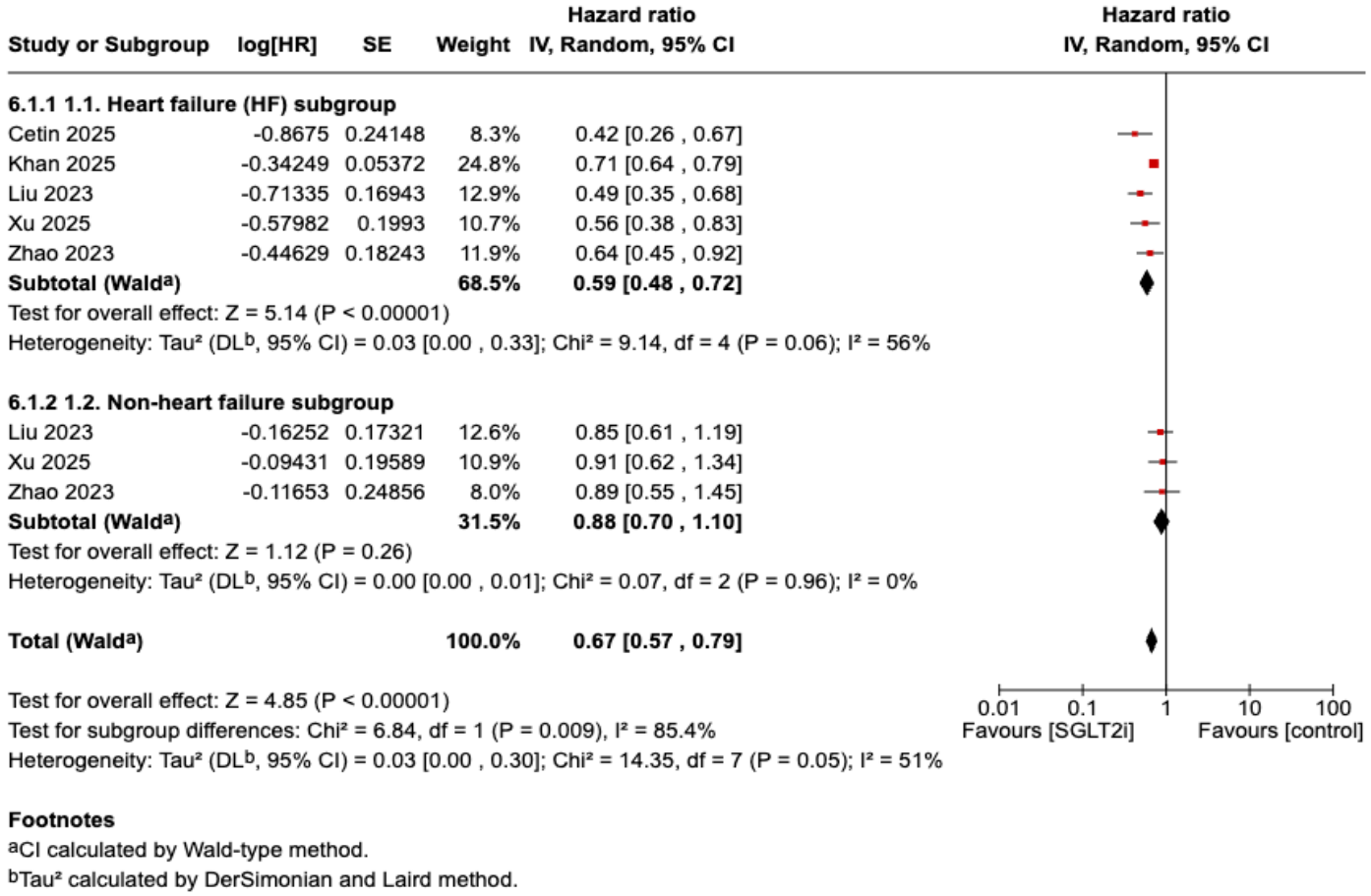


Figure 3. This forest plot represents a meta-analysis of non-diabetic patients receiving SGLT2 inhibitors vs no SGLT2 inhibitors after catheter ablation for atrial fibrillation (AF). SGLT2 inhibitors reduce the risk of AF recurrence by ~59% after ablation in non-diabetic patients.

Results



Study or Subgroup	log[HR]	SE	Weight	Hazard ratio IV, Random, 95% CI
6.1.1 1.1. Heart failure (HF) subgroup				
Cetin 2025	-0.8675	0.24148	8.3%	0.42 [0.26 , 0.67]
Khan 2025	-0.34249	0.05372	24.8%	0.71 [0.64 , 0.79]
Liu 2023	-0.71335	0.16943	12.9%	0.49 [0.35 , 0.68]
Xu 2025	-0.57982	0.1993	10.7%	0.56 [0.38 , 0.83]
Zhao 2023	-0.44629	0.18243	11.9%	0.64 [0.45 , 0.92]
Subtotal (Wald[a])			**68.5%**	**0.59 [0.48 , 0.72]**
Test for overall effect: Z = 5.14 (P < 0.00001)				
Heterogeneity: Tau² (DL[b], 95% CI) = 0.03 [0.00 , 0.33]; Chi² = 9.14, df = 4 (P = 0.06); I² = 56%				
6.1.2 1.2. Non-heart failure subgroup				
Liu 2023	-0.16252	0.17321	12.6%	0.85 [0.61 , 1.19]
Xu 2025	-0.09431	0.19589	10.9%	0.91 [0.62 , 1.34]
Zhao 2023	-0.11653	0.24856	8.0%	0.89 [0.55 , 1.45]
Subtotal (Wald[a])			**31.5%**	**0.88 [0.70 , 1.10]**
Test for overall effect: Z = 1.12 (P = 0.26)				
Heterogeneity: Tau² (DL[b], 95% CI) = 0.00 [0.00 , 0.01]; Chi² = 0.07, df = 2 (P = 0.96); I² = 0%				
Total (Wald[a])			**100.0%**	**0.67 [0.57 , 0.79]**
Test for overall effect: Z = 4.85 (P < 0.00001)				
Test for subgroup differences: Chi² = 6.84, df = 1 (P = 0.009), I² = 85.4%				
Heterogeneity: Tau² (DL[b], 95% CI) = 0.03 [0.00 , 0.30]; Chi² = 14.35, df = 7 (P = 0.05); I² = 51%				

Footnotes

[a]CI calculated by Wald-type method.

[b]Tau² calculated by DerSimonian and Laird method.

Figure 4. Effect of SGLT2 inhibitors on atrial fibrillation recurrence after catheter ablation stratified by heart failure status. This demonstrates significant reduction in AF recurrence among patients with heart failure treated with SGLT2 inhibitors (HR 0.59, 95% CI 0.48-0.72; P < 0.00001), while no significant effect was observed in patients without heart failure (HR 0.88, 95% CI 0.70-1.10; P = 0.26). The interaction test indicated a statistically significant subgroup difference (P = 0.009), suggesting that the therapeutic benefit of SGLT2 inhibitors is predominantly confined to patients with heart failure.

Results

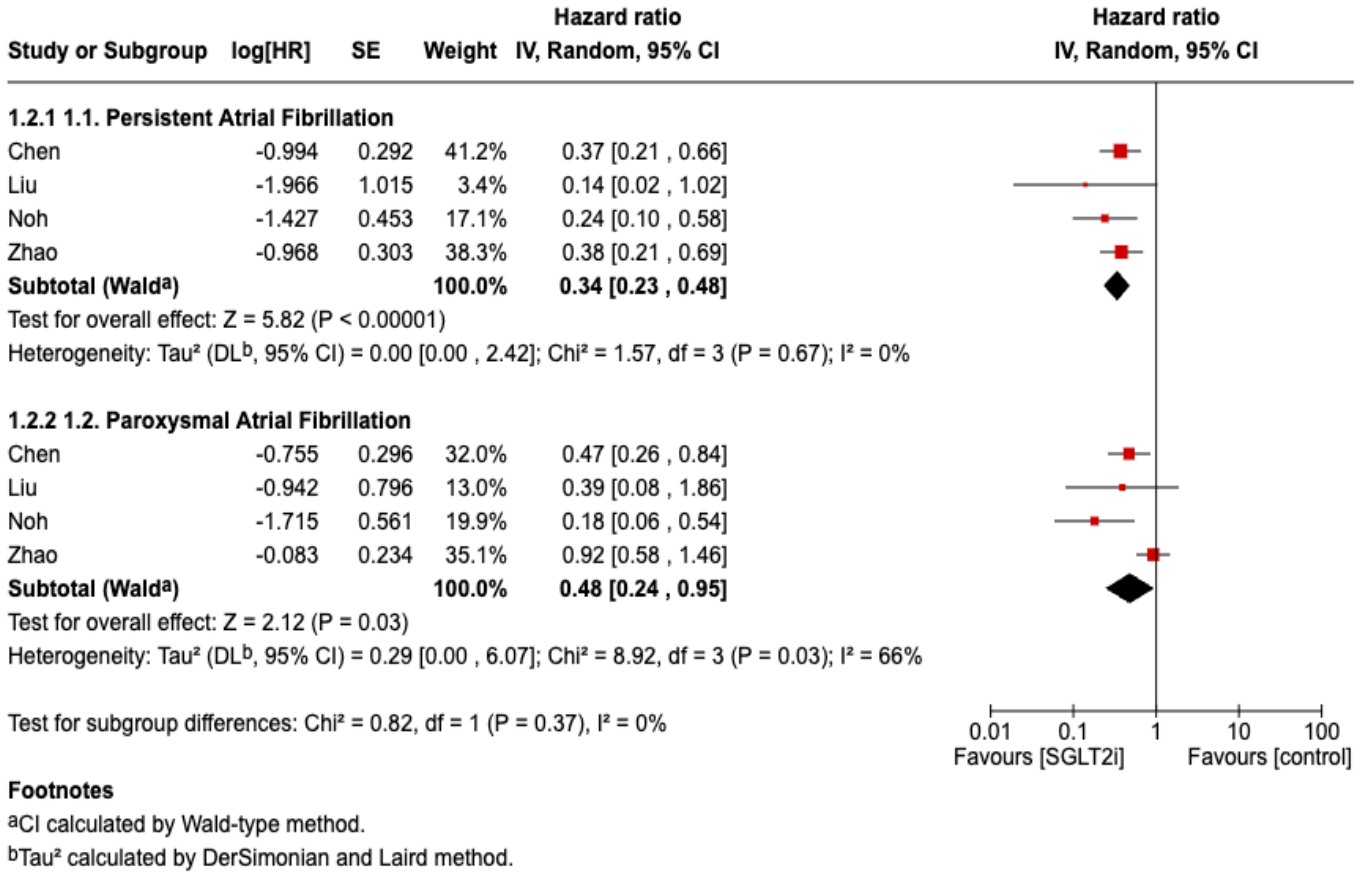


Figure 5. Forest plot of AF recurrence between SGTL2i and control group based on AF type. Subgroup analyses showed benefit in persistent AF (HR 0.34, 95% CI 0.23–0.48; P < 0.00001; I^2 = 0%) and paroxysmal AF (HR 0.48, 95% CI 0.24–0.95; P = 0.03; I^2 = 66%).

Results

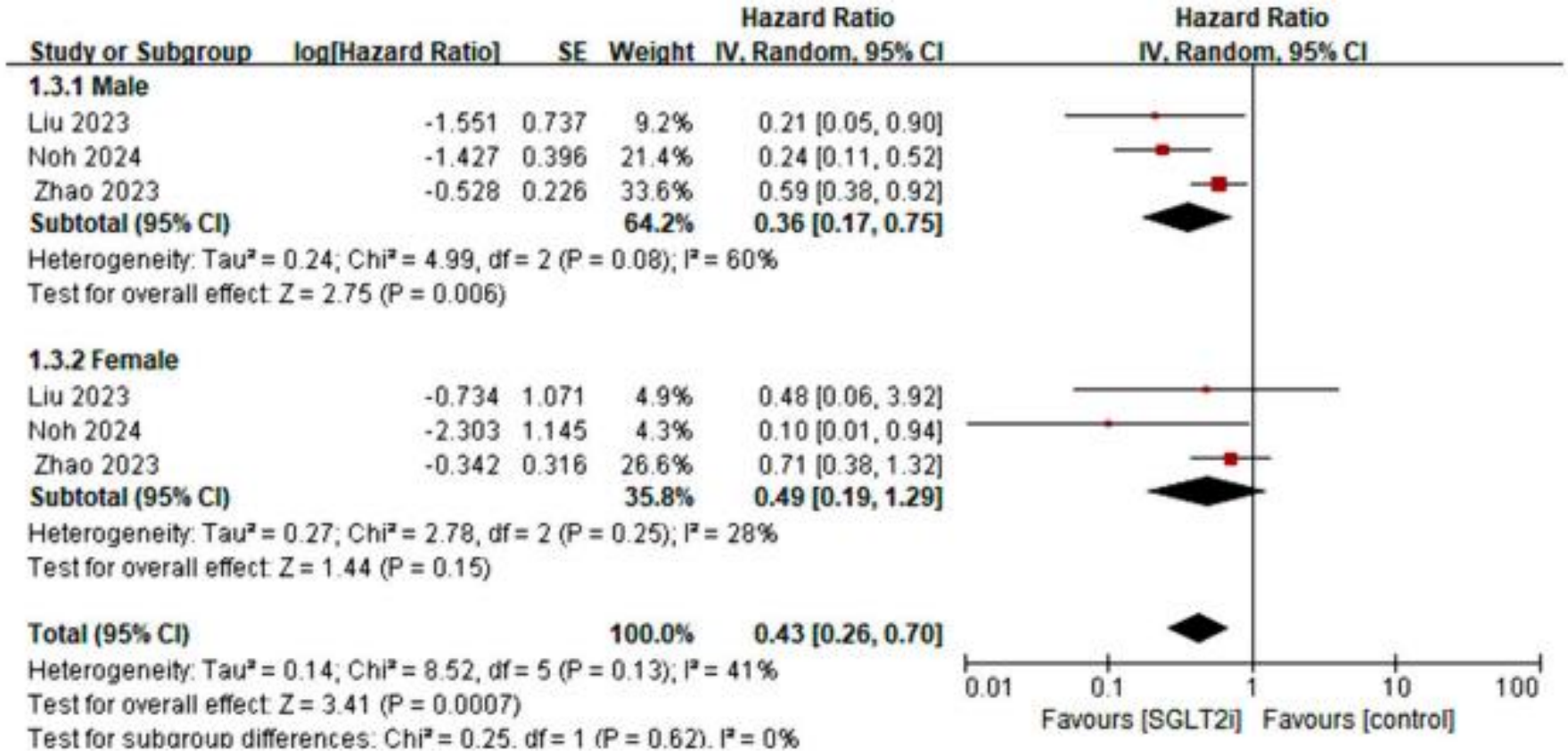


Figure 6. Forest plot of AF recurrence between SGTL2i and control group based on sex. A significant effect was observed in males (HR 0.36, 95% CI 0.17–0.75; P = 0.006), while the reduction in females was not statistically significant (HR 0.49, 95% CI 0.19–1.29; P = 0.15).

Risk of bias assessment

Included studies	Selection (0-4 points)				Comparability (0-2 points)		Outcome (0-3 points)			Total points
	Exposed cohort	Non-exposed cohort	Ascertainment of exposure	Outcome of interest	Adjust for the important risk factors	Adjust for other risk factors	Assessment of outcomes	Follow up length	Loss to follow-up rate	
Khan 2025	*	*	*	*	*	*	*	*	*	9
Xu 2025	*	*	*	*	*	*	*	*	*	9
Zhao 2023	*	*	*	*	*		*	*	*	8
Abu Qaoud 2023	*	*	*		*	*		*	*	7
Chen 2025	*	*	*	*		*	*	*	*	8
Cetin 2025	*	*	*	*			*	*	*	7
Liu 2023	*	*	*	*	*		*	*	*	8
Noh 2024	*	*	*	*	*		*	*	*	8
Luo 2024	*	*	*	*	*			*	*	7

Table 2. Risk of bias assessment for included observational studies using the Newcastle-Ottawa Scale (NOS). The NOS evaluates study quality across three domains; selection of participants (0-4 points), comparability of study groups (0-2 points) and outcome assessment (0-3 points) with a maximum score of 9 indicating highest methodological rigor. Most studies demonstrated high-quality design (scores ≥7), reflecting appropriate cohort selection, adequate adjustment for confounding variables, objective outcome assessment and sufficient follow-up duration.

Risk of bias assessment

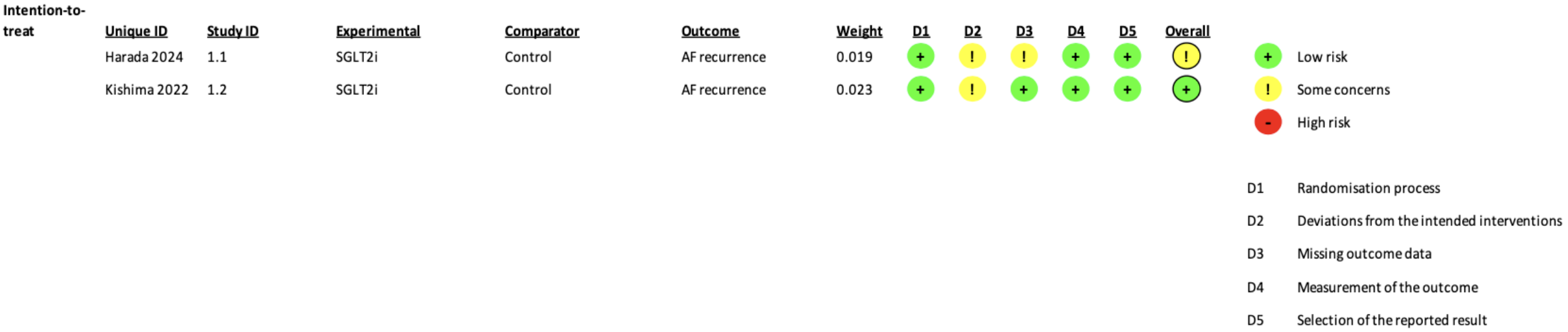


Figure 7. Risk-of-bias assessment using the ROB-2 tool for included randomized controlled trials. Domains related to randomization, outcome measurement and reporting showed predominantly low risk of bias while minor concerns persisted in deviations from intended interventions and missing outcome data, resulting in an overall judgment of some concerns.

Discussion

- Meta-analysis of 11 studies (19,059 patients) showed SGLT2 inhibitors reduce AF recurrence by 46% after ablation supporting an emerging role for these agents beyond glycemic regulation.
- SGLT2 inhibitors promote natriuresis and reduce cardiac filling pressures which help decrease atrial stretch and lower the likelihood of triggering arrhythmias [10].
- Due to the anti-inflammatory and antifibrotic properties of SGLT2 inhibitors, this may reduce structural changes in atrial tissue, a key contributor to AF recurrence [11]. Together, these effects support the biological plausibility of the reduced recurrence rates observed in our pooled data.
- One of the most notable findings was the substantial benefit in non-diabetic patients who experienced a reduction in recurrence similar to those with diabetes. This indicates that the effects of SGLT2 inhibitors extend well beyond glucose lowering and likely stem from broader cardiovascular benefits. Another study also observed improvements in arrhythmia outcomes independent of diabetic status reinforcing this therapeutic benefit [3].

Discussion

- Patients with heart failure showed a marked reduction in AF recurrence when treated with SGLT2 inhibitors. The significant interaction observed in our analysis suggests that the hemodynamic and metabolic effects of SGLT2 inhibitors may be particularly relevant in the setting of impaired ventricular function. Similar findings were reported in another study with improved rhythm outcomes in heart failure patients undergoing catheter ablation[7].
- Patients with persistent AF experienced greater improvement compared with those with paroxysmal AF. This aligns with the concept that persistent AF is more strongly driven by structural remodeling and fibrosis processes that SGLT2 inhibitors may help mitigate [4]. These findings suggest that patients with more advanced atrial disease may derive the greatest advantage from this therapy.
- Men experienced a statistically significant reduction in AF recurrence whereas the effect in women did not reach significance. Although the reasons for this are unclear, it may relate to differences in atrial substrate or hormonal influences. Another study also reported stronger responses in male cohorts which is consistent with our findings [13]. However, further studies are needed to better understand this discrepancy.

Limitations

Despite these promising results, several limitations must be acknowledged:

- Most of the included studies were retrospective or cohort-based, which introduces the possibility of residual confounding and selection bias despite adjustment for known variables.

- Definitions of AF recurrence, methods of detection, and follow-up duration varied considerably across studies contributing to the observed heterogeneity.

- Randomized controlled trials were limited and therefore, larger prospective trials are necessary to validate these associations and to more precisely identify patient groups that may derive the greatest therapeutic advantage.

Conclusion

- The overall findings suggest that SGLT2 inhibitors may serve as an effective adjunct therapy to improve rhythm outcomes after AF ablation.

- Even though most studies were observational, the consistent findings and large number of patients make the results reliable and clinically meaningful.

References

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Thank you