



Efficacy and Safety of Ablation for Symptomatic Atrial Fibrillation in Elderly Patients: A Meta-Analysis

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Specialty section:

This article was submitted to
Cardiovascular Therapeutics,
a section of the journal
Frontiers in Cardiovascular Medicine

Received: 30 June 2021

Accepted: 16 August 2021

Published: 20 September 2021

Citation:

Lee W-C, Wu P-J, Chen H-C,
Fang H-Y, Liu P-Y and Chen M-C
(2021) Efficacy and Safety of Ablation
for Symptomatic Atrial Fibrillation in
Elderly Patients: A Meta-Analysis.
Front. Cardiovasc. Med. 8:734204.
doi: 10.3389/fcvm.2021.734204

Background: Age affects the efficacy of pharmacological treatment for atrial fibrillation (AF). Catheter ablation, including radiofrequency (RF) or cryoballoon ablation, is an effective strategy for symptomatic AF. This meta-analysis aimed to analyze the efficacy and safety of AF ablation in elderly patients with AF compared to non-elderly patients with AF.

Methods: We searched several databases for articles published between January 1, 2008 and March 31, 2020. Eighteen observational studies with 21,039 patients were analyzed. Data including recurrence of AF or atrial tachyarrhythmia (ATA), complications, procedural time, and fluoroscopic time were compared between the elderly and non-elderly groups.

Results: The elderly patients had significantly higher incidences of recurrent AF or ATA after AF ablation compared to the non-elderly patients (<60 years old) (odds ratio [OR], 1.21; 95% confidence interval [CI], 1.11–1.33). The elderly patients had significantly higher incidences of complications of AF ablation compared to the non-elderly patients (OR, 1.37; 95% CI, 1.14–1.64). However, elderly AF patients with age ≥ 75 years old had similar incidence of recurrent AF or ATA and complication after AF ablation compared to non-elderly patients with AF.

Conclusions: The elderly patients had significantly higher incidences of recurrent AF or ATA and complications after ablation for non-paroxysmal AF compared to non-elderly patients with AF (<60 years old), except in patients ≥ 75 years old.

Keywords: elderly, atrial fibrillation, radiofrequency ablation, cryoballoon ablation, recurrence

INTRODUCTION

As the elderly population grows and the quality of the healthcare system improves, the burden of treating elderly patients with atrial fibrillation (AF) increases gradually (1, 2). However, higher ischemic risks and less effectiveness of antiarrhythmic medications are expected in elderly patients with AF (3, 4). Therefore, there is still a big challenge for physicians to treat elderly patients with AF. In addition, the elderly patients with AF tend to have a large left atrium with electrical and structural remodeling and fibrosis, which also reduce the efficacy of pharmacological treatment

(5, 6). Catheter ablation has recently emerged as an important therapeutic strategy to achieve and maintain a normal sinus rhythm in symptomatic patients with AF (7, 8). Moreover, catheter ablation for AF has been reported to reduce mortality and HF readmission in patients with heart failure (HF) (9). The prevalence of HF was higher in the elderly population than in the younger population (10). However, the efficacy and safety of catheter ablation in elderly patients with AF have not been clearly explored. Previous studies comparing the outcomes of AF ablation between elderly and non-elderly populations had different criteria for elderly or different age distribution and had inconsistent results. This study aimed to explore the efficacy and safety of AF ablation in elderly patients with AF compared to non-elderly patients with AF.

METHODS

Search Strategies, Trial Selection, Quality Assessment, Review Process, and Data Extraction

Systematic literature searches for published articles between January 1, 2008 and December 31, 2020, in PubMed, Embase, Cochrane Library, ProQuest, ScienceDirect, ClinicalKey, Web of Science, and ClinicalTrials.gov were separately performed by two cardiologists. The keywords “elderly,” “atrial fibrillation ablation,” “radiofrequency ablation,” “cryoballoon ablation,” and “efficacy” were used. We did not set language restrictions to increase the number of eligible articles, and disagreements were resolved by a third reviewer. Only randomized controlled trials and clinical studies that compared the clinical outcomes between elderly and non-elderly groups of different age distributions after non-valvular AF ablation were included in the present

meta-analysis. The inclusion criteria were human studies with a parallel design. The exclusion criteria included conference abstracts, case reports or series, animal studies, and review articles. **Figure 1** illustrates the literature search and screening protocol. Our search identified 258 articles after removing duplicates. Among them, 18 observational and cohort studies with 21,039 participants met our inclusion criteria and were included in this study.

Assessment of Risk of Bias in the Included Studies

The risk of bias in the included studies was appraised by two independent reviewers (WC Lee and PJ Wu) according to the Risk Of Bias In Non-Randomized Studies Of Interventions (ROBINS-I) tool, with disagreements resolved by consensus or by arbitration with a third author (HY Fang). The ROBINS-I requires the assessment of the following domains: bias due to confounding, bias in selection of participants into the study, bias in measurement of exposure, bias in Departures from exposure, bias due to missing data, bias in measurement of the outcome, and bias in selection of the reported result.

Statistical Analysis

All analyses were performed using the Comprehensive Meta-Analysis software, version 3 (Biostat Inc., Englewood, NJ, USA) and Cochrane RevMan software (version 5.4.1). The frequency of each evaluated outcome was extracted from each study and was presented as the cumulative rate. The standardization of each evaluated result originated from each study was presented as standardized mean differences (SMDs). A random-effects model was used to pool individual odds ratios (ORs). The chi-square test was used to evaluate heterogeneity across trials ($p \leq 0.1$,

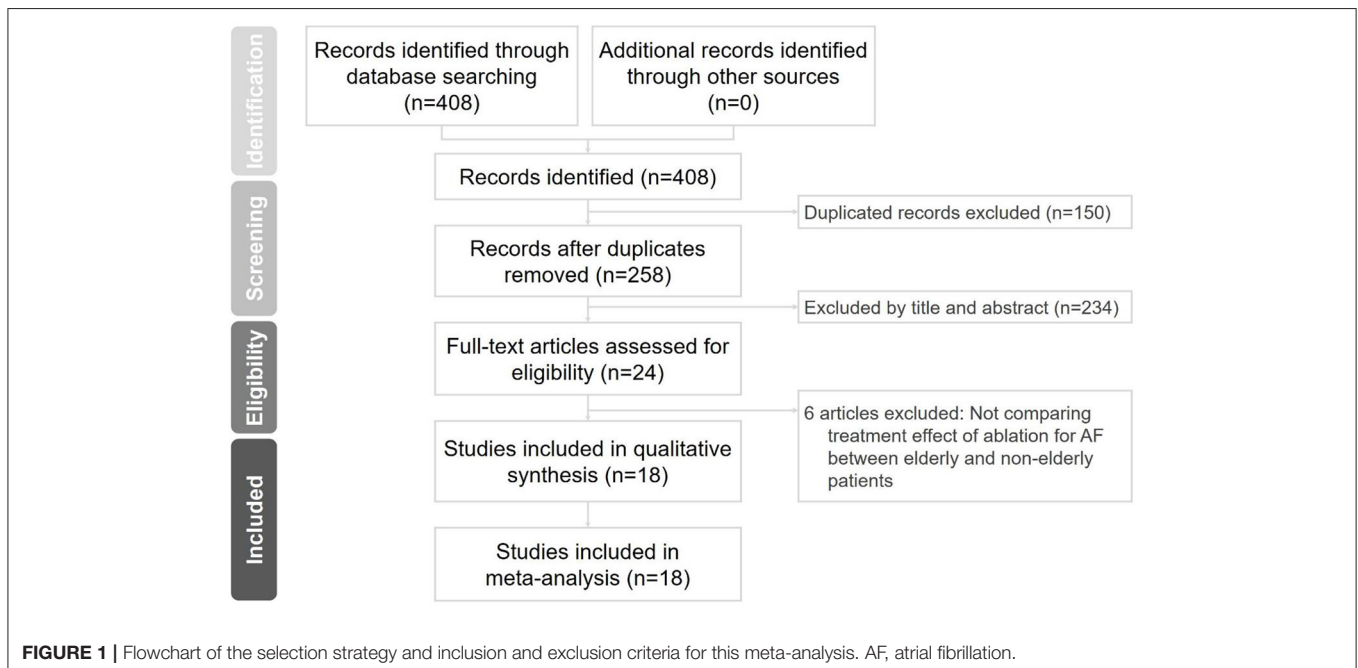


TABLE 1 | Characteristics of the 18 included studies.

The definition of elderly	First author (year)	Patients number (male %)	Age (years)	Study period	The prevalence of PAF (%)	Study design	Ablation method
≥60 years old	Bhargava et al. (11)	323 (80.2)	54 ± 12	N/A	53.8	Cohort study	RF ablation
	Liu et al. (12)	7,926 (70.0)	56 ± 10	1998–2009	80.0	Cohort study	RF ablation
≥65 years old	Leong-Sit et al. (13)	1,548 (76.8)	56 ± 22	2000/11–2008/9	64.8	Cohort study	RF ablation
	Guiot et al. (14)	1,016 (71.7)	62 ± 11	2001–2009	60.3	Cohort study	RF ablation
	Lioni et al. (15)	316 (56.3)	57 ± 12	N/A	100	Cohort study	RF ablation
	Kis et al. (16)	390 (73.1)	N/A (20.5% >65 y/o)	2001/3–2011/12	90.3	Cohort study	RF ablation or cryoballoon ablation
	Traub et al. (17)	60 (73.3)	58 ± 14	2003/2–2007/2	100	Cohort study	RF ablation
≥70 years old	Kautzner et al. (18)	3,197 (68.2)	59 ± 10	2001/1–2016/12	77.6	Cohort study	RF ablation
	Zado et al. (19)	1,165 (77.3)	55 ± 11	2000/11–2007/7	64.0	Cohort study	RF ablation
≥75 years old	Kusumoto et al. (20)	240 (72.1)	66 ± 10	2004/12–2006/12	62.1	Cohort study	RF ablation
	Abugattas et al. (21)	159 (54.1)	65 ± 12	2012/6–2016/2	100	Cohort study	Cryoballoon ablation
	Tscholl et al. (22)	80 (57.5)	75 ± 12	N/A	46.3	Cohort study	Cryoballoon ablation
	Abdin et al. (23)	238 (60.9)	65 ± 11	2015/7–2017/3	38.2	Cohort study	Cryoballoon ablation
	Heeger et al. (24)	208 (51.0)	70 ± 10	N/A	57.2	Cohort study	Cryoballoon ablation
	Bunch et al. (25)	752 (58.6)	65 ± 11	2005/3–2008/5	53.7	Cohort study	RF ablation
≥80 years old	Tan et al. (26)	377 (N/A)	72 ± 8	2006/1–2007/10	42.2	Cohort study	RF ablation
	Santangeli et al. (27)	2,754 (69.3)	63 ± 22	2008–2011	28.9	Cohort study	RF ablation
	Kanda et al. (28)	290 (57.9)	69 ± 11	N/A	100	Cohort study	Cryoballoon ablation

PAf, paroxysmal atrial fibrillation; RF, radiofrequency; N/A, not available.

considered significant). I^2 statistics (>50% was considered significant heterogeneity) was used to examine each outcome. Funnel plots and Egger's test were used to assess potential publication bias ($p \leq 0.1$ was considered significant). Statistical significance was set at $p < 0.05$.

RESULTS

Characteristics of Included Studies

The study selection process is displayed in **Figure 1**, and 18 studies met the inclusion criteria. In total, 21,039 participants were included. The definition of elderly in each study, participant characteristics, study period, and ablation method are shown in **Table 1**. The definition of elderly or age distribution differed between enrolled studies including those aged ≥60 (11, 12), ≥65 (13–16), ≥70 (17, 18), ≥75 (19–24), and ≥80 (25–28) years. One study with RF ablation and cryoballoon ablation was excluded in the analysis for ablation method and procedural complications (16).

Risk of Bias Assessment

The risk of bias of included studies, according to the ROBINS-I tool, was moderate in eight studies (11, 13, 14, 16, 17, 19, 24, 28), serious in six studies (15, 21–23, 25, 27), and critical in four investigation (12, 18, 20, 26) (**Supplementary Table 1**).

Patient Demographics

Table 2 describes the basic demographics and comorbidities of study patients. The elderly group was older (elderly group vs. non-elderly group; 68.7 ± 6.8 years vs. 56.3 ± 13.3 years,

TABLE 2 | Patient demographics.

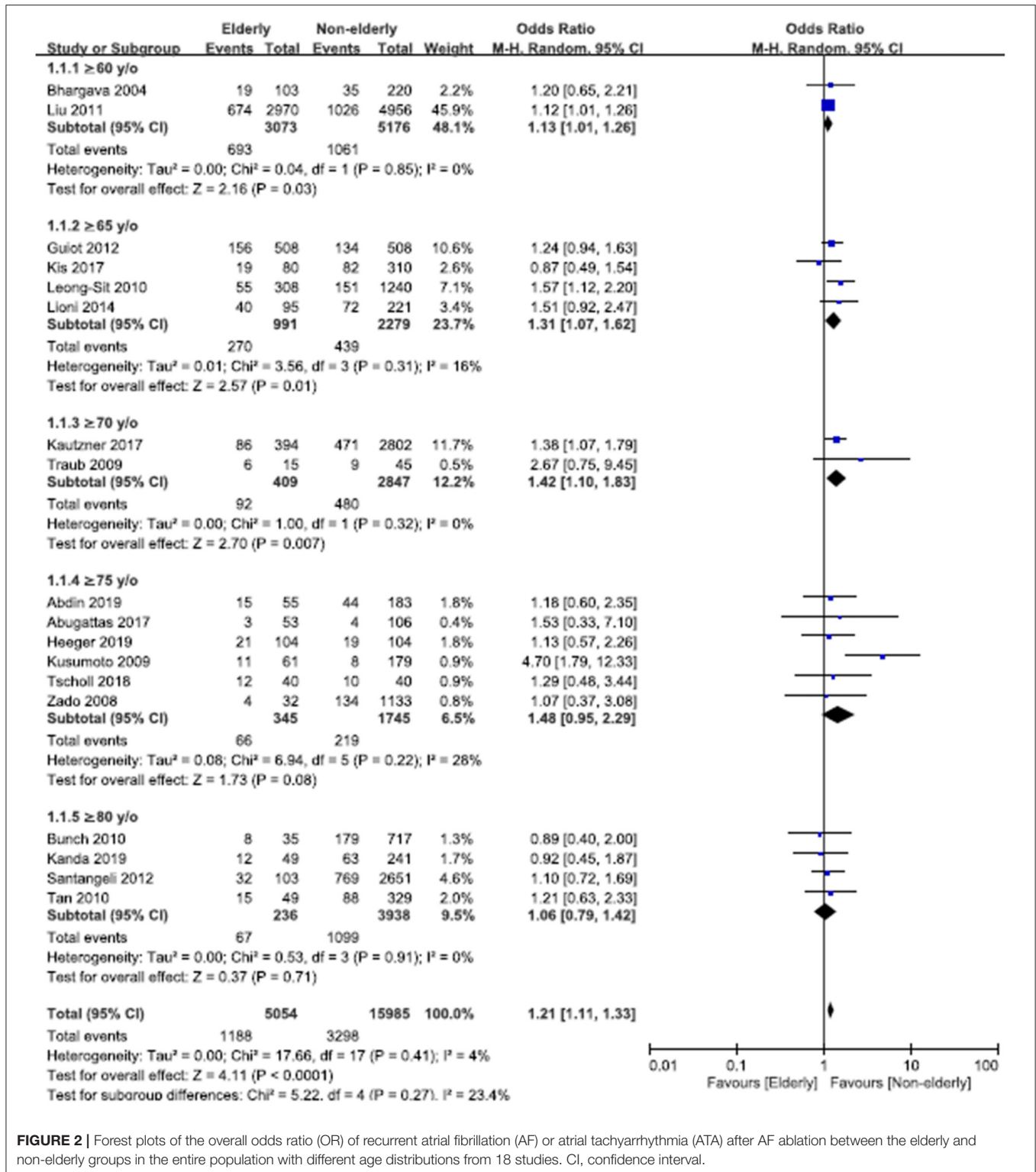
	Elderly (5,054)	Non-elderly (15,985)	p-value
Age (years)	68.7 ± 6.8 (4,666)	56.3 ± 13.3 (14,435)	<0.001
Male sex, % (number)	61.0 (3,053)	72.2 (11,306)	<0.001
Diabetes mellitus % (number)	13.1 (174)	10.4 (905)	0.003
Hypertension % (number)	64.6 (979)	47.2 (4,877)	<0.001
Heart failure % (number)	12.9 (159)	10.7 (1,018)	0.020
Coronary artery disease % (number)	17.5 (268)	9.4 (741)	<0.001
Paroxysmal AF % (number)	79.0 (3,995)	64.8 (10,352)	<0.001

Data are expressed as mean ± standard deviation or as percentage (number). AF, atrial fibrillation.

$p < 0.001$) and had fewer male patients (elderly group vs. non-elderly group; 61.0 vs. 72.2%, $p < 0.001$). The elderly group had significantly higher prevalence of diabetes mellitus, hypertension, heart failure, coronary artery disease, and paroxysmal AF compared to the non-elderly group.

Pooled Odds Ratio of Recurrent Atrial Fibrillation or Atrial Tachyarrhythmia After Ablation in the Elderly vs. Non-elderly Groups

The overall OR of recurrent AF or atrial tachyarrhythmia (ATA) after ablation in the elderly vs. non-elderly groups was 1.21 (95% confidence interval [CI], 1.11–1.33; **Figure 2**), with non-significant heterogeneity (Chi^2 , 17.66; df , 17; I^2 , 4%; $p = 0.41$) and



non-significant publication bias according to Egger regression (t , 1.33; df , 16; p = 0.20) on inspection of the funnel plot (Supplementary Figure 1). In the subgroup analysis of age ≥ 60 , ≥ 65 , ≥ 70 , ≥ 75 , and ≥ 80 years, the ORs (95% CI) of recurrent

AF or ATA after ablation in the elderly vs. non-elderly groups were 1.13 (1.01–1.26), 1.31 (1.07–1.62), 1.42 (1.10–1.83), 1.48 (0.95–2.29), and 1.06 (0.79–1.42), respectively. There was non-significant heterogeneity in the subgroups of patients aged ≥ 60 ,

≥ 65 , ≥ 70 , ≥ 75 , and ≥ 80 years. There was no publication bias according to Egger regression on inspection of the funnel plot in the subgroups of age ≥ 60 (t , 0.44; df , 2; p = 0.71), ≥ 75 (t , 0.60; df , 4; p = 0.58), and ≥ 80 years (t , 1.02; df , 2; p = 0.42) (Supplementary Figures 2–4).

Pooled Odds Ratio of Recurrent Atrial Fibrillation or Atrial Tachyarrhythmia in Different Subgroups in Terms of Ablation Methods and Types of AF

In terms of different ablation methods, the OR of recurrent AF or ATA after radiofrequency (RF) ablation in the elderly vs. non-elderly group was 1.29 (95% CI, 1.12–1.48; **Figure 3A**), with non-significant heterogeneity (Chi^2 , 15.67; df , 11; I^2 , 30%; p = 0.15) but significant publication bias according to Egger regression (t , 1.96; df , 10; p = 0.08) on inspection of the funnel plot (Supplementary Figure 5). In the subgroup analysis of age ≥ 60 , ≥ 65 , ≥ 70 , ≥ 75 , and ≥ 80 years, the ORs (95% CI) of recurrent AF or ATA after RF ablation in the elderly vs. non-elderly groups were 1.13 (1.01–1.26), 1.38 (1.14–1.68), 1.42 (1.10–1.83), 2.28 (0.53–9.78), and 1.09 (0.79–1.51), respectively. There was no publication bias according to Egger regression on inspection of the funnel plot in the subgroups of age ≥ 65 (t , 0.88; df , 1; p = 0.54) and ≥ 80 years (t , 0.52; df , 1; p = 0.70) (Supplementary Figures 6, 7).

However, the OR of recurrent AF or ATA after cryoballoon ablation in the elderly vs. non-elderly group was 1.12 (95% CI, 0.78–1.61; **Figure 3B**), with non-significant heterogeneity (Chi^2 , 0.57; df , 4; I^2 , 0%; p = 0.97) and non-significant publication bias according to Egger regression (t , 1.46; df , 3; p = 0.24) on inspection of the funnel plot (Supplementary Figure 8). In the subgroup analysis of age ≥ 75 and ≥ 80 years, the ORs (95% CI) of recurrent AF or ATA after cryoballoon ablation in the elderly vs. non-elderly groups were 1.21 (0.79–1.83) and 0.92 (0.45–1.87), respectively. There was significant publication bias according to Egger regression on inspection of the funnel plot in the subgroups of age ≥ 75 (t , 5.33; df , 2; p = 0.03) (Supplementary Figure 9).

In the subgroups of mixed-type (paroxysmal and non-paroxysmal) AF, the OR of recurrent AF or ATA after AF ablation in the elderly vs. non-elderly groups was 1.22 (95% CI, 1.09–1.36; **Figure 4**), with non-significant heterogeneity (Chi^2 , 14.64; df , 13; I^2 , 11%; p = 0.33) and non-significant publication bias according to Egger regression (t , 0.96; df , 12; p = 0.35) on inspection of the funnel plot (Supplementary Figure 10). In the subgroups of paroxysmal AF, the OR of recurrent AF or ATA after ablation in the elderly vs. non-elderly groups was 1.38 (95% CI, 0.95–2.01; **Figure 4**), with non-significant heterogeneity (Chi^2 , 2.45; df , 3; I^2 , 0%; p = 0.48) and non-significant publication bias according to Egger regression (t , 0.42; df , 2; p = 0.71) on inspection of the funnel plot (Supplementary Figure 11).

Pooled Odds Ratios of Complications of AF Ablation

The overall OR of complications of AF ablation in the elderly vs. non-elderly group was 1.37 (95% CI, 1.14–1.64; **Figure 5**), with non-significant heterogeneity (Chi^2 , 6.26; df , 13; I^2 , 0%;

p = 0.94) and non-significant publication bias according to Egger regression (t , 0.03; df , 12; p = 0.97) on inspection of the funnel plot (Supplementary Figure 12). In the subgroups analysis of age ≥ 60 , ≥ 65 , ≥ 70 , ≥ 75 , and ≥ 80 years old, the ORs (95% CI) of complications of AF ablation in the elderly vs. non-elderly groups were 1.30 (1.00–1.68), 1.85 (1.09–3.12), 1.69 (1.05–2.73), 1.00 (0.50–1.97), and 1.00 (0.23–4.27), respectively. In the subgroups of age ≥ 75 years old, there was non-significant heterogeneity (Chi^2 , 1.48; df , 5; I^2 , 0%; p = 0.92) and non-significant publication bias according to Egger regression (t , 0.52; df , 4; p = 0.63) on inspection of the funnel plot (Supplementary Figure 13).

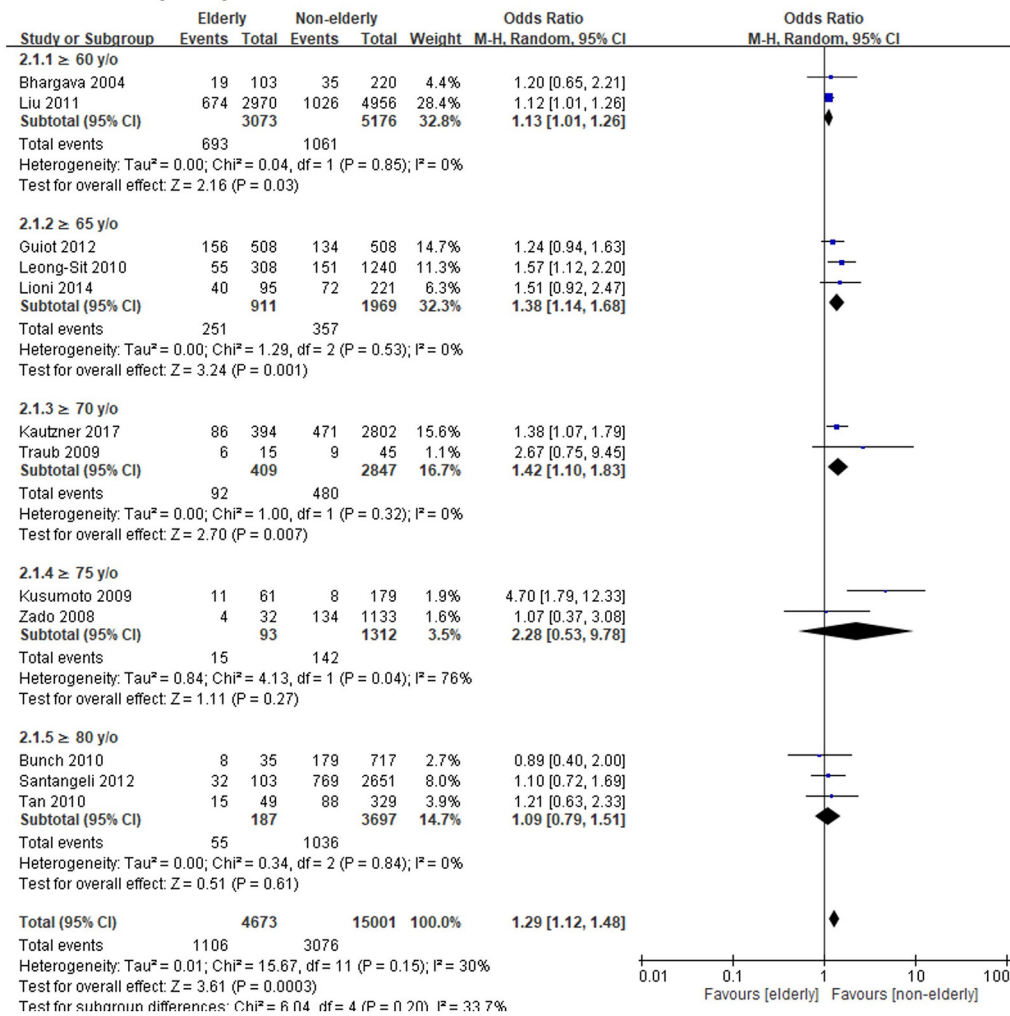
In terms of ablation methods, the OR of complications of RF ablation in the elderly vs. non-elderly group was 1.40 (95% CI, 1.16–1.68; **Figure 6A**), with non-significant heterogeneity (Chi^2 , 4.27; df , 9; I^2 , 0%; p = 0.89) and non-significant publication bias according to Egger regression (t , 0.96; df , 8; p = 0.36) on inspection of the funnel plot (Supplementary Figure 14). The OR of complications of cryoballoon ablation in the elderly vs. non-elderly group was 0.95 (95% CI, 0.45–1.99; **Figure 6B**), with non-significant heterogeneity (Chi^2 , 1.00; df , 3; I^2 , 0%; p = 0.80) and non-significant publication bias according to Egger regression (t , 0.62; df , 2; p = 0.60) on inspection of the funnel plot (Supplementary Figure 15).

Standardized Mean Differences of Procedural Time and Fluoroscopic Time of AF Ablation Between the Elderly and Non-elderly Groups

According to nine studies, the SMD of procedural time of AF ablation in the elderly vs. non-elderly group was -0.04 (95% CI, -0.16 – 0.09 ; **Figure 7A**), with significant heterogeneity (Chi^2 , 19.34; df , 8; I^2 , 59%; p = 0.01) but non-significant publication bias according to Egger regression (t , 1.53; df , 7; p = 0.17) on inspection of the funnel plot (Supplementary Figure 16). In terms of different ablation methods, the SMD of procedural time of RF ablation for AF in the elderly vs. non-elderly group was -0.06 (95% CI, -0.21 – 0.09 ; **Figure 7A**), with significant heterogeneity (Chi^2 , 7.54; df , 3; I^2 , 60%; p = 0.06) and non-significant publication bias according to Egger regression (t , 2.74; df , 2; p = 0.11) on inspection of the funnel plot (Supplementary Figure 17). The SMD of procedural time of cryoballoon ablation for AF in the elderly vs. non-elderly group was -0.02 (95% CI, -0.26 – 0.22 ; **Figure 7A**), with significant heterogeneity (Chi^2 , 10.70; df , 4; I^2 , 63%; p = 0.03) but non-significant publication bias according to Egger regression (t , 0.03; df , 3; p = 0.98) on inspection of the funnel plot (Supplementary Figure 18).

According to nine studies, the SMD of fluoroscopic time of AF ablation in the elderly vs. non-elderly group was -0.03 (95% CI, -0.18 – 0.13 ; **Figure 7B**), with significant heterogeneity (Chi^2 , 28.26; df , 8; I^2 , 72%; p = 0.0004) but non-significant publication bias according to Egger regression (t , 1.17; df , 7; p = 0.28) on inspection of the funnel plot (Supplementary Figure 19). In terms of different ablation methods, the SMD of fluoroscopic time of RF ablation for AF in the elderly vs. non-elderly group

A Radiofrequency ablation



B Cryoballoon ablation

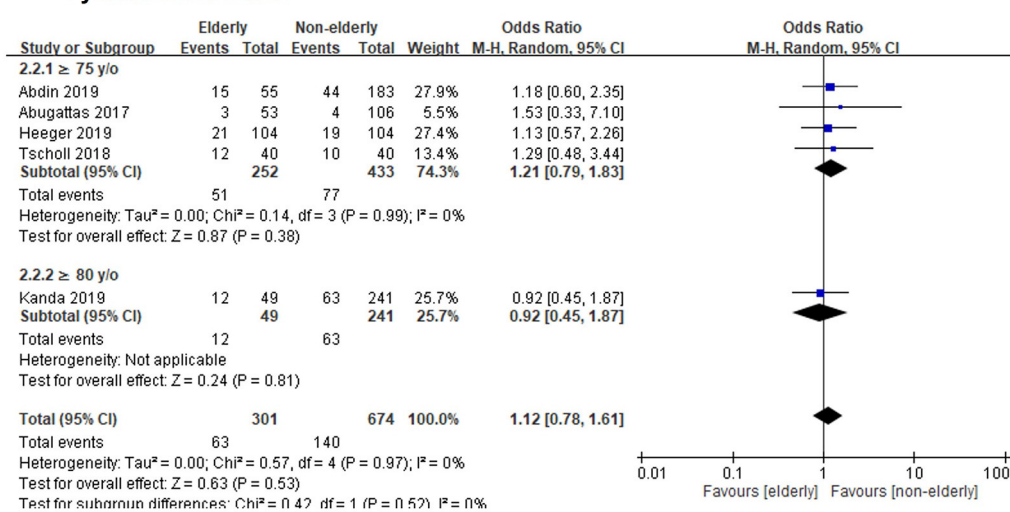


FIGURE 3 | Forest plots of the OR of recurrent AF or ATA after radiofrequency (RF) ablation (A) or cryoballoon ablation (B) between elderly and non-elderly groups from 17 studies with different age stratification.

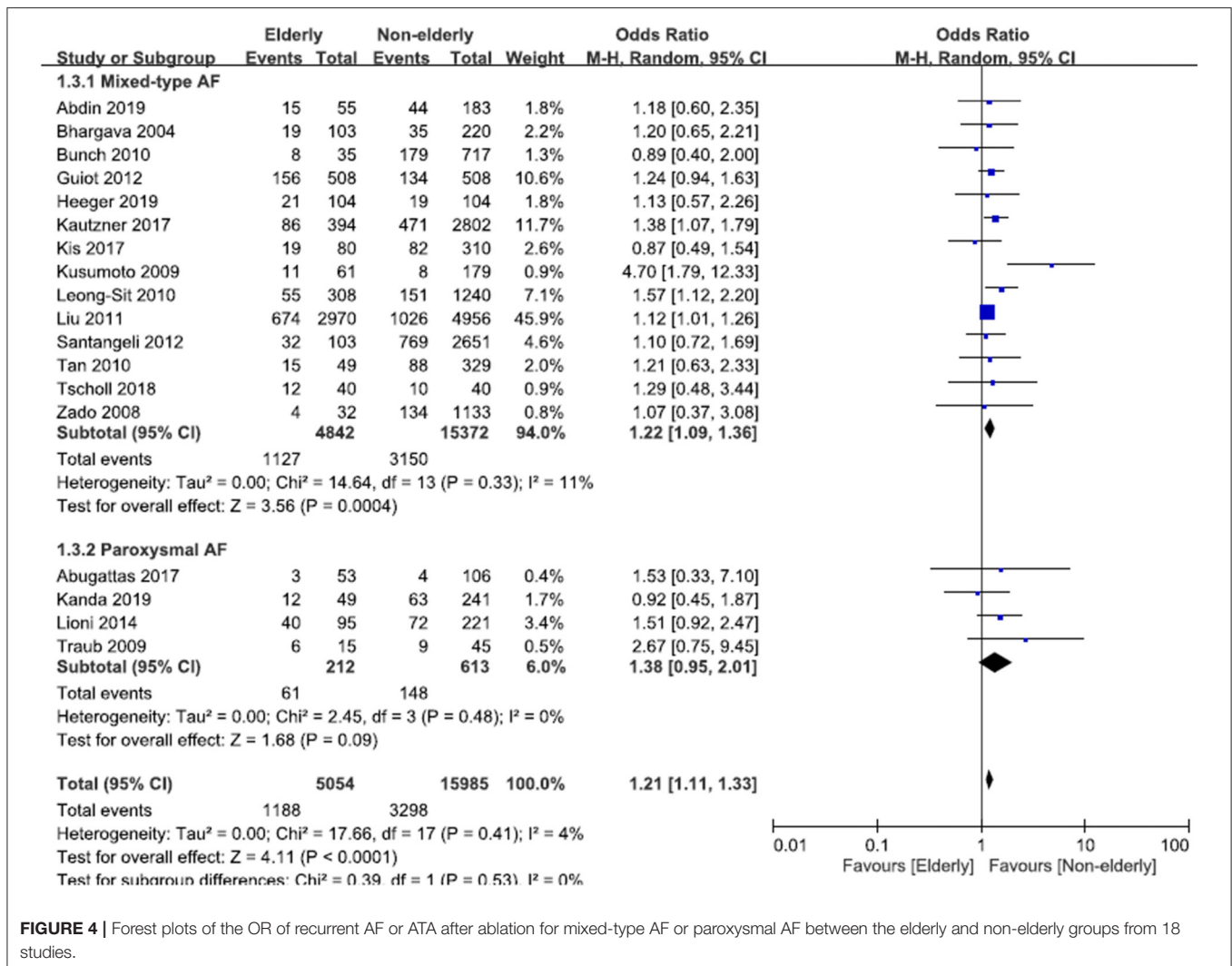


FIGURE 4 | Forest plots of the OR of recurrent AF or ATA after ablation for mixed-type AF or paroxysmal AF between the elderly and non-elderly groups from 18 studies.

was 0.02 (95% CI, -0.22-0.26; **Figure 7B**), with significant heterogeneity (Chi², 19.94; *df*, 3; I², 85%; *p* = 0.0002) but non-significant publication bias according to Egger regression (*t*, 2.24; *df*, 2; *p* = 0.15) on inspection of the funnel plot (**Supplementary Figure 20**). The SMD of fluoroscopic time of cryoballoon ablation for AF in the elderly group vs. non-elderly group was -0.07 (95% CI, -0.28-0.14; **Figure 7B**), with significant heterogeneity (Chi², 8.28; *df*, 4; I², 52%; *p* = 0.08) but non-significant publication bias according to Egger regression (*t*, 0.24; *df*, 3; *p* = 0.82) on inspection of the funnel plot (**Supplementary Figure 21**).

DISCUSSION

This meta-analysis study showed that elderly patients with AF had a significantly higher incidence of recurrent AF or ATA after AF ablation compared to non-elderly patients with AF (<60 years old), except in patients ≥75 years old. Compared to non-elderly patients with AF, elderly patients with AF had a significantly higher incidence of recurrent AF or ATA after AF

ablation for mixed-type (paroxysmal and non-paroxysmal) AF. However, there was no difference in terms of recurrent AF or ATA after AF ablation for paroxysmal AF between elderly and non-elderly patients with AF. The elderly patients with AF had a significantly higher incidence of complication of AF ablation compared to non-elderly patients with AF, except in patients ≥75 years old. There was no difference in the procedure time and fluoroscopic time between elderly and non-elderly patients with AF. The elderly group had significantly higher prevalence of diabetes mellitus, hypertension, heart failure, coronary artery disease, and paroxysmal AF compared to the non-elderly group. Except for age, more comorbidities also influenced the incidence of recurrent AF or ATA after AF ablation.

AF is a progressive and an important disease in the elderly population. In addition, age has a great impact in the development of AF and imposes significant limitations in the treatment of AF because of the higher prevalence of conduction abnormalities that limits the use of pharmacological rate or rhythm control strategies (29). AF ablation is effective in achieving and maintaining sinus rhythm, and is associated

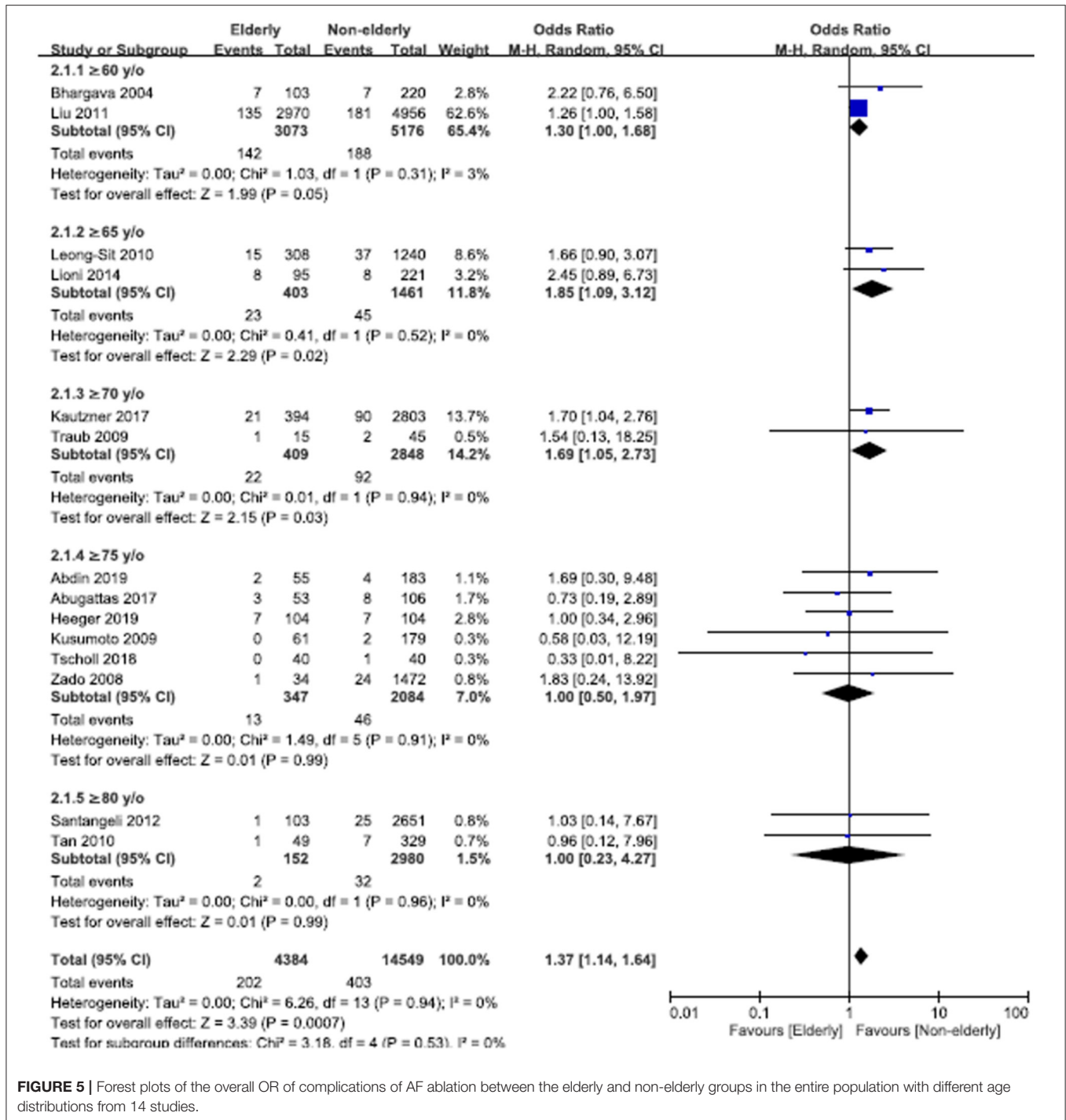


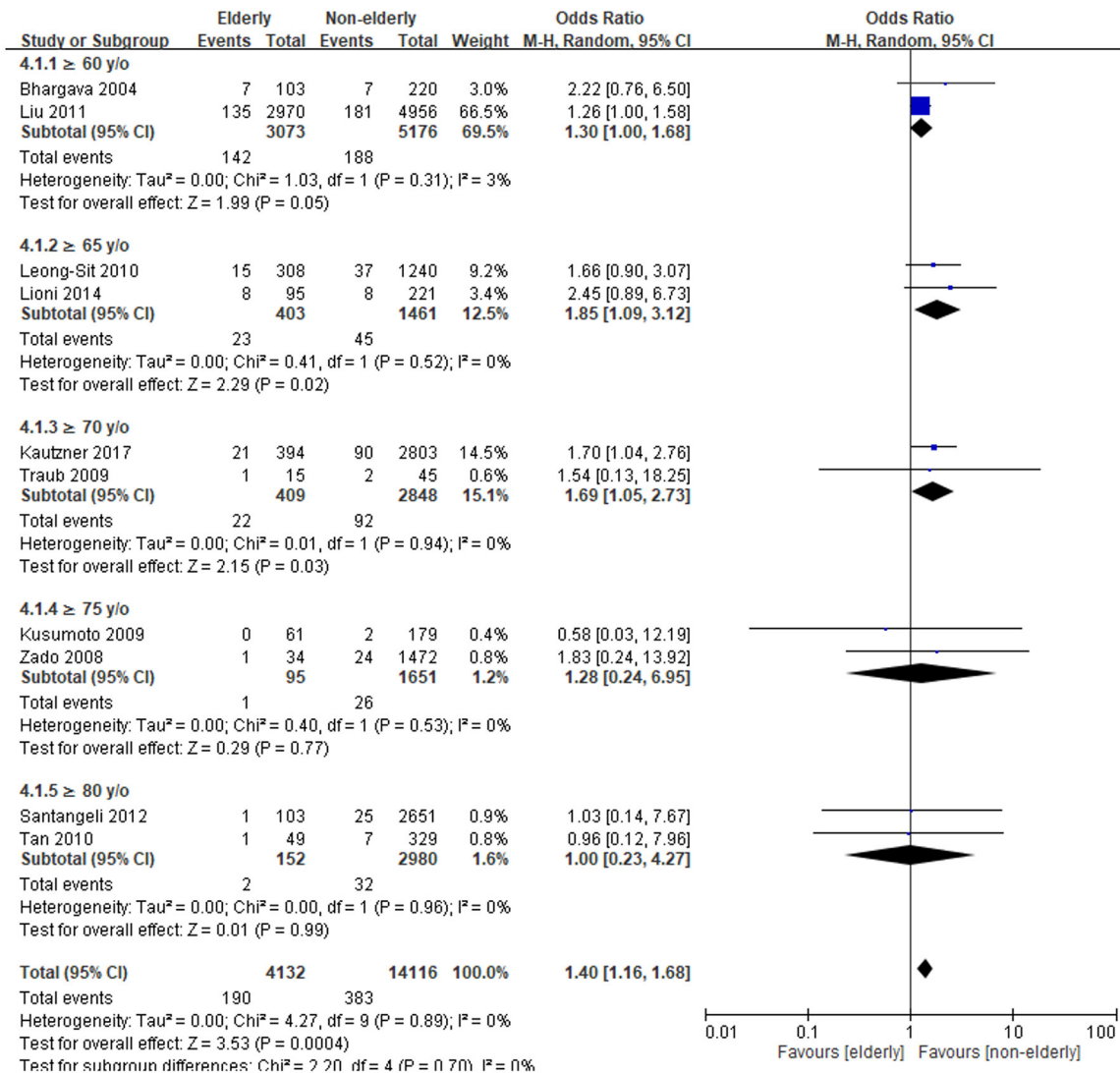
FIGURE 5 | Forest plots of the overall OR of complications of AF ablation between the elderly and non-elderly groups in the entire population with different age distributions from 14 studies.

with lower mortality, improved quality of life, and a lower risk of progression to permanent AF (29, 30). Ablation is an effective strategy in treating symptomatic AF in selected elderly patients as a stand-alone therapy or as hybrid therapy with anti-arrhythmic medication, and is associated with decreased healthcare resource utilization in all age groups (19, 20). The current guidelines recommended ablation strategy for patients with symptomatic AF associated with heart failure and not specific comment of

ablation strategy for the elderly patients (7, 8). Traditionally, the definition of elderly was aged 60 or 65 years and over (31). Recently, some researchers redefined elderly as age ≥75 years old (32).

Many papers reported similar efficacy of AF ablation (11, 12, 14–16, 18–28), and similar safety in elderly patients (15–28). Leong-Sit et al. reported a relatively lower complication rate and higher possibilities in freedom from AF off anti-arrhythmic

A Radiofrequency ablation



B Cryoballoon ablation

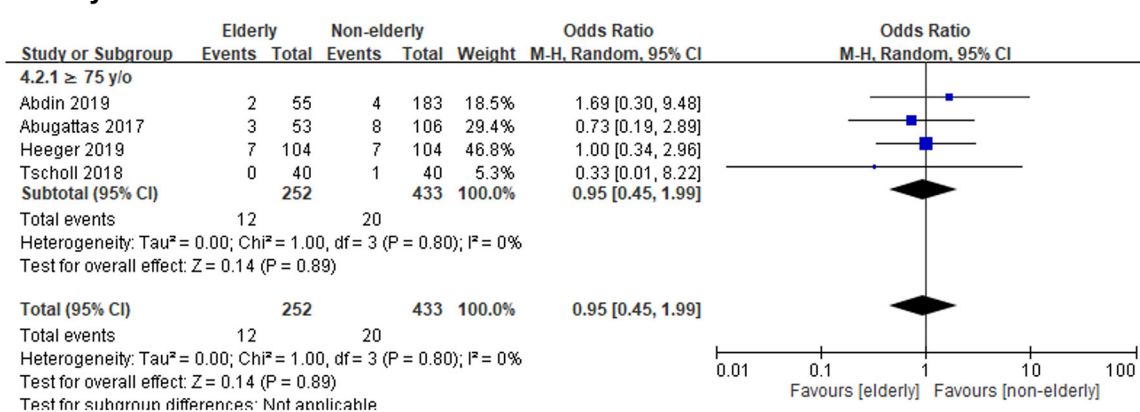
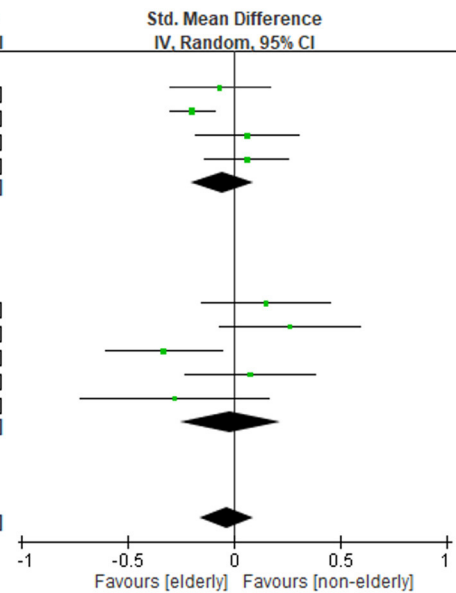


FIGURE 6 | Forest plots of the OR of complications of RF ablation (A) or cryoballoon ablation (B) between the elderly and non-elderly groups in the entire population from 14 studies with different age stratification.

A Procedural time

Study or Subgroup	Elderly			Non-elderly			Weight	Std. Mean Difference	
	Mean	SD	Total	Mean	SD	Total		IV, Random, 95% CI	95% CI
5.1.1 RF ablation									
Bhargava 2004	4.64	0.99	103	4.71	1.03	220	12.2%	-0.07	[-0.30, 0.17]
Kautzner 2017	3.56	1.138	394	3.79	1.162	2803	18.3%	-0.20	[-0.30, -0.09]
Lioni 2014	3.499	0.629	95	3.457	0.75	221	11.9%	0.06	[-0.18, 0.30]
Santangeli 2012	2.617	0.767	103	2.533	1.433	2651	13.9%	0.06	[-0.14, 0.26]
Subtotal (95% CI)			695			5895	56.2%	-0.06	[-0.21, 0.09]
Heterogeneity: Tau ² = 0.01; Chi ² = 7.54, df = 3 (P = 0.06); I ² = 60%									
Test for overall effect: Z = 0.76 (P = 0.44)									
5.1.2 Cryoballoon ablation									
Abdin 2019	1.69	0.542	55	1.627	0.373	183	9.5%	0.15	[-0.15, 0.45]
Abugattas 2017	1.182	0.487	53	1.078	0.345	106	8.6%	0.26	[-0.07, 0.59]
Heeger 2019	1.542	0.375	104	1.667	0.375	104	10.5%	-0.33	[-0.61, -0.06]
Kanda 2019	1.45	0.467	49	1.417	0.433	241	9.3%	0.08	[-0.23, 0.38]
Tscholl 2018	2.083	0.383	40	2.175	0.248	40	5.9%	-0.28	[-0.72, 0.16]
Subtotal (95% CI)			301			674	43.8%	-0.02	[-0.26, 0.22]
Heterogeneity: Tau ² = 0.05; Chi ² = 10.70, df = 4 (P = 0.03); I ² = 63%									
Test for overall effect: Z = 0.16 (P = 0.88)									
Total (95% CI)			996			6569	100.0%	-0.04	[-0.16, 0.09]
Heterogeneity: Tau ² = 0.02; Chi ² = 19.34, df = 8 (P = 0.01); I ² = 59%									
Test for overall effect: Z = 0.58 (P = 0.56)									
Test for subgroup differences: Chi ² = 0.07, df = 1 (P = 0.79), I ² = 0%									



B Fluoroscopic time

Study or Subgroup	Elderly			Non-elderly			Weight	Std. Mean Difference	
	Mean	SD	Total	Mean	SD	Total		IV, Random, 95% CI	95% CI
6.1.1 RF ablation									
Bhargava 2004	86.6	20.99	103	88.84	28.2	220	12.1%	-0.09	[-0.32, 0.15]
Kautzner 2017	11.4	8.6	394	13.7	11.1	2803	15.7%	-0.21	[-0.32, -0.11]
Lioni 2014	19.34	13.83	95	15.52	11.12	221	11.8%	0.32	[0.08, 0.56]
Santangeli 2012	58	22	103	55	28	2651	13.2%	0.11	[-0.09, 0.30]
Subtotal (95% CI)			695			5895	52.7%	0.02	[-0.22, 0.26]
Heterogeneity: Tau ² = 0.05; Chi ² = 19.94, df = 3 (P = 0.0002); I ² = 85%									
Test for overall effect: Z = 0.16 (P = 0.87)									
6.1.2 Cryoballoon ablation									
Abdin 2019	24.6	34.1	55	21.6	34.6	183	10.1%	0.09	[-0.21, 0.39]
Abugattas 2017	13.2	5.2	53	14.6	6.4	106	9.4%	-0.23	[-0.56, 0.10]
Heeger 2019	17.8	5.25	104	19.1	4.65	104	10.9%	-0.26	[-0.53, 0.01]
Kanda 2019	25.9	9.5	49	23.7	9	241	9.9%	0.24	[-0.07, 0.55]
Tscholl 2018	22.9	7.8	40	24.5	5.75	40	7.0%	-0.23	[-0.67, 0.21]
Subtotal (95% CI)			301			674	47.3%	-0.07	[-0.28, 0.14]
Heterogeneity: Tau ² = 0.03; Chi ² = 8.28, df = 4 (P = 0.08); I ² = 52%									
Test for overall effect: Z = 0.66 (P = 0.51)									
Total (95% CI)			996			6569	100.0%	-0.03	[-0.18, 0.13]
Heterogeneity: Tau ² = 0.03; Chi ² = 28.26, df = 8 (P = 0.0004); I ² = 72%									
Test for overall effect: Z = 0.33 (P = 0.74)									
Test for subgroup differences: Chi ² = 0.31, df = 1 (P = 0.58), I ² = 0%									

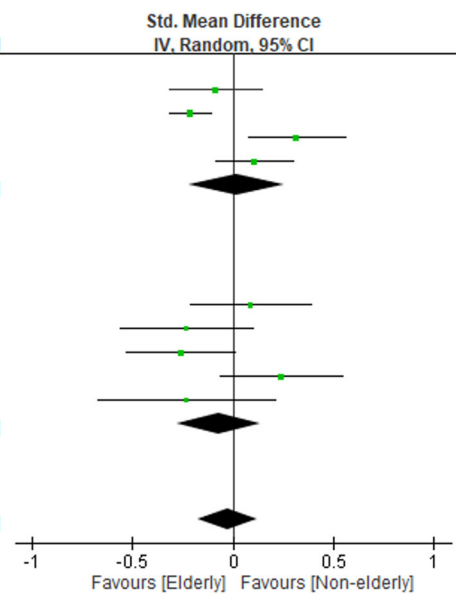


FIGURE 7 | (A) Forest plots of the standardized mean differences (SMDs) of procedural time of RF ablation or cryoballoon ablation in the elderly vs. non-elderly group from nine studies. **(B)** Forest plots of the SMDs of fluoroscopic time of RF ablation or cryoballoon ablation in the elderly vs. non-elderly group from nine studies.

medication in the younger population (<45 years old) (13). This population (<45 years old) presented significantly smaller left atrial size and zero point of CHADS2 score, indicating less structural and electrical remodeling of the left atrium. Kautzner et al. also reported a significantly higher prevalence of good arrhythmia control without anti-arrhythmic medication in the younger population (<70 years old vs. >70 years old; 58.2 vs. 44.2%; *p* < 0.001) (18). Guiot et al. also reported that age >75

years was the only predictor of cerebrovascular events after AF ablation in patients ≥65 years old (14). However, all studies were observational studies, and most had limited patient numbers. Of note, in this study, we found that elderly AF patients with age ≥75 years old had similar incidence of recurrent AF or ATA and complication after AF ablation compared to non-elderly patients with AF (<60 years old). However, elderly patients with AF (60–74 years old) had a significantly higher incidence

of recurrent AF or ATA and complication after AF ablation compared to non-elderly patients with AF (<60 years old). The mechanisms responsible for discrepancy remain unexplored. Most aged patients had structural and electrical remodeling in left atrium due to longer AF duration and had more comorbidities (5, 12, 15). After ablation, the degree of reverse electrical and structural remodeling of the left atrium may be influenced by longer AF duration and more comorbidities (33). In addition, a higher prevalence of AF or ATA originating from the non-pulmonary vein triggers in the aged population could contribute to the recurrence of AF or ATA by ablation strategy with pulmonary vein isolation alone. However, more ablation to include non-pulmonary vein triggers may increase the risk of complications.

LIMITATIONS

This study has several limitations. First, all studies were observational cohort studies and not all studies provided detailed information about the AF ablation procedure. Second, the age distribution in each study was not the same. However, a total of 21,039 participants were enrolled from 18 studies. The present study provides important findings on the outcomes of AF ablation in the elderly population with AF. However, large and randomized studies are warranted to validate these findings.

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CONCLUSION

The elderly patients with AF had significantly higher incidences of recurrent AF or ATA and complications after ablation for non-paroxysmal AF compared to the non-elderly patients with AF (<60 years old). However, the efficacy and safety of AF ablation in AF patients ≥ 75 years old were similar to those of non-elderly patients with AF.

DATA AVAILABILITY STATEMENT

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

AUTHOR CONTRIBUTIONS

W-CL and P-JW reviewed the articles and wrote the manuscript. H-YF and H-CC prepared figures. P-YL and M-CC did the final revision. All authors reviewed the manuscript.

SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: <https://www.frontiersin.org/articles/10.3389/fcvm.2021.734204/full#supplementary-material>

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