

Predictors of late atrial fibrillation recurrence after cryoballoon-based pulmonary vein isolation: a meta-analysis

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Abstract

Background: The recurrence rate of atrial fibrillation (AF) after cryoballoon ablation in drug refractory AF patients is high. Late-recurrence of AF has various predictors.

Aim: The aim of the study was to explore the related risk factors that can effectively predict late AF recurrence after cryoballoon-based pulmonary vein isolation.

Methods: The PubMed and Web of Science databases were searched from 1 January 2013 to 1 August 2016, and studies were chosen that met the pre-stated inclusion criteria. The reference lists of the retrieved articles were also reviewed. Two authors independently extracted information on the designs of the studies. The strength of the relationship between different risk factors and late recurrence was assessed by the adjusted hazard ratio.

Results: A total of 16 papers met the inclusion criteria and were included in the meta-analysis. The hazard ratio of late atrial arrhythmia recurrence in patients with early recurrence was 4.19 compared with the reference group (95% CI 2.73–6.44, $p < 0.00001$); that of increased left atrial diameter was 1.25 (95% CI 1.12–1.3, $p < 0.0001$); that of a long duration of AF before ablation was 1.10 (95% CI 1.04–1.17, $p < 0.0009$); and that of persistent AF was 2.44 (95% CI 1.30–4.58, $p < 0.006$). However, there exists significant heterogeneity for each indicator, and a slight publication bias was observed.

Conclusions: Our study suggests that early recurrence in the blanking period, increased left atrial size, a long duration of AF before ablation and persistent AF are independent predictors of late recurrence after cryoballoon ablation.

Key words: cryoballoon ablation, atrial fibrillation, late recurrence, predictors

Kardiol Pol 2017; 75, 4: 376–385

INTRODUCTION

Currently, pulmonary vein isolation (PVI) is an important percutaneous catheter ablation method for treating drug-resistant paroxysmal atrial fibrillation (AF). In recent years, cryoballoon (CB) ablation has appeared as a new option to treat AF [1]. Although the ablation strategies and equipment continue to improve, there are still many patients suffering from AF recurrence, repeat ablation, and further ablation fail. Because of the different demographics of patients and the inherent risk of catheter ablation, it has become especially important to screen high-risk patients after catheter ablation and assess their prognosis following the corresponding treatment. Previous studies have reported that persistent AF could predict the late

recurrence of AF (LRAF) after radiofrequency (RF) ablation [2], and several recent meta-analyses have demonstrated that RF ablation and CB ablation share similar safety and effectiveness [3]. Therefore, the purpose of this article was to research the risk factors of LRAF after CB ablation to better support its clinical application.

METHODS

Search strategy

PubMed and Web of Science were searched systematically for all articles published between 1 January 2013 and 1 August 2016, without any restriction, using the following terms in their titles, abstracts, or keyword lists: “cryoballoon

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Received: 04.05.2016

Accepted: 29.11.2016

Available as AoP: 27.12.2016

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ablation", "cryoablation", "atrial fibrillation", "paroxysmal atrial fibrillation", "persistent atrial fibrillation", "recurrence", "predictor", "cohort studies", and "observational study". This search strategy was performed iteratively until no new relevant article was found.

Study selection

Studies were considered eligible if they met the following criteria: (a) the study design was a cohort study; (b) the study mentioned predictors of the LRAF after CB ablation; (c) the hazard ratio (HR) and corresponding 95% confidence interval (CI) (or data to calculate them) were reported; (d) the study had more than three months of follow-up; and (e) the study populations were patients with persistent AF or paroxysmal AF.

Reviews, editorials, meeting abstracts, and commentaries were excluded from our analysis. Studies were excluded if they did not provide HR and the corresponding 95% CI or a way to calculate the standard error. The articles were also excluded if the endpoint was not the LRAF, if the surgical strategy was RF ablation or laser ablation, or if the articles were written in a language other than English.

Definitions

All documented AF episodes of > 30 s after the index procedure were considered as a recurrence. We defined early recurrence of AF or atrial tachycardia as occurring < three months following ablation (usually considered as a "blanking period"). Late recurrence was defined as recurrence of AF/atrial tachycardia with a duration > 30 s occurring three months after the index ablation procedure [4]. Repeat ablation at any time was classified as a recurrence. AF duration was defined as the duration of arrhythmia since the first diagnosis.

Data extraction

Data were abstracted independently by two reviewers, who reached consensus on all details. We extracted the following information from each article: first authors, published year, country, age range, total patients, study design, type of CB ablation, end point event, duration of follow-up, type of AF, independent risk factors and adjusted HR estimates and corresponding 95% CI, characteristics of the study population and age at baseline, body mass index, coronary artery disease, early recurrence of AF (ERAF), left atrial diameter (LAD), duration of AF and number of persistent patients and the late recurrence rates.

Statistical analysis

If multivariate HR was provided, they were used for statistical analyses, with preference given to the univariate HR. Studies were transformed to the log (RRs) to stabilise the variances and normalise the distribution. A HR > 1 indicated a high rate of late recurrence in patients with risk factors; conversely, a HR < 1 indicated a low rate of late recurrence. For the meta-analysis, both the fixed-effects model (weighted with

inverse variance) and the random-effects model were considered according to heterogeneity. If there was heterogeneity, the following methods were used to explore the source of heterogeneity: (a) subgroup analysis and (b) sensitivity analysis performed by excluding the trials that potentially biased the results. If heterogeneity still existed, the random-effects model was used. Subgroup analyses were carried out based on the AF type, and the HRs of paroxysmal AF and persistent AF were analysed separately. All risk factors in the meta-analysis were continuous. To evaluate the heterogeneity across studies, I^2 , as derived from the χ^2 test, was used to describe the percentage of the variability in effect estimates resulting from heterogeneity, rather than sampling error. An $I^2 > 50\%$ indicated at least moderate statistical heterogeneity. Potential publication bias was assessed by a visual inspection of the funnel plots in which the log HR was plotted against their standard errors. A p value < 0.05 was considered statistically significant, unless specified otherwise. All statistical analyses were performed using Review Manager, version 5.3.

RESULTS

Literature search and study characteristics

The search strategy generated 188 references from PubMed (n = 89) and Web of Science (n = 99). After excluding non-compliant documents, only 16 articles were included in this study. In the remaining 16 articles [4–19], ERAF, LAD, AF duration, and persistent AF were mentioned 14, eight, six, and four times, respectively. There were three retrospective studies, 12 prospective studies, and one case-control study in the final 16 articles. Five of them were from Belgium, two were from Germany, one was from Slovakia, and eight were from Turkey. All of the risk factors were analysed using quantitative data. The search process is detailed in Figure 1, and the characteristics of the sixteen included articles and the patients are summarised in Tables 1 and 2.

Follow-up

The follow-up strategies in analysed studies were similar. After discharge from the hospital, enrolled patients were scheduled for visits in the outpatient clinics at one, three, six, and 12 months after ablation and then every six months thereafter. Twenty-four-hour Holter recordings were obtained at each follow-up visit. Clinical follow-up was obtained for all patients in all studies.

Procedural outcomes

Figure 2 shows the results from the random-effects model combining the HR of ERAF. Among 14 studies, five showed a significantly positive relation between ERAF and LRAF in paroxysmal AF patients, three in persistent AF, and six in both paroxysmal AF and persistent AF patients. The HR for the association varied from 1.37 to 60 across the studies. Overall, compared with the control group, patients with ERAF experienced a significantly increased risk for developing LRAF

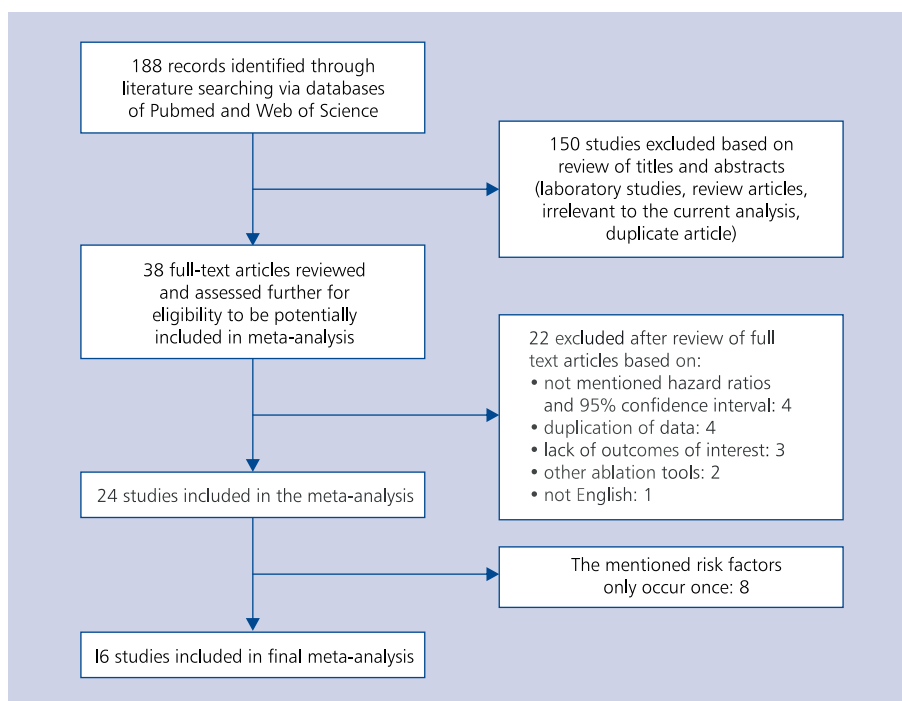


Figure 1. Flow diagram of the literature search and study selection

Table 1. Characteristics of patients included in the meta-analysis

First author	Age [years]	Female N (%)	BMI [kg/m ²]	CAD N (%)	ERAF N (%)	LAD [mm]	Duration of AF history [months]	Persistent AF N (%)	LRAF N (%)
Mugnai [4]	56.7 ± 13.3	104 (31)	26.7 ± 4.3	25 (8)	29 (8.7)	41.9 ± 7.4	18.9 ± 14.1	0	48 (14.5)
Irfan [5]	57.7 ± 12.9	122 (31)	27.1 ± 4.5	30 (8)	71 (18.1)	41.6 ± 7.0	24.7 ± 18.1	62 (16)	71 (18.1)
Koektuerk [6]	63.0 ± 10.0	20 (20)	NA	15 (15)	24 (24)	NA	5.5 ± 3.7	100 (100)	33 (33)
Canpolat (1) [7]	49.2 ± 7.6	17 (41.5)	27.5 ± 5.2	NA	10 (24.4)	37.4 ± 3.3	60 (24–96)	0	9 (21.9)
Boho [8]	57.0 ± 8.8	60 (29.3)	30.0 ± 4.7	31 (15.1)	NA	48.3 ± 5.2	NA	58 (28.3)	NA
Canpolat (2) [9]	53.5 ± 10.9	175 (43.5)	24.5 ± 3.8	37 (9.2)	41 (10.2)	37.8 ± 4.9	74.4 ± 54.0	77 (19.2)	95 (23.4)
Ciconte (1) [10]	62.4 ± 9.8	14 (28)	27.5 ± 3.4	2 (4)	14 (28)	46.0 ± 7.2	32.7 ± 37.6	299 (100)	20 (40)
Ciconte (2) [11]	59.6 ± 12.0	50 (34.97)	NA	16 (11)	26 (18.2)	43.6 ± 7.2	31.3 ± 48.8	30 (20.98)	28 (19.6)
Gurses [12]	55.4 ± 10.6	152 (50.8)	24.7 ± 3.1	32 (10.70)	46 (15.40)	38.7 ± 3.8	72 (12–360)	57 (19.10)	70 (23.41)
Aytemir (1) [13]	55.4 ± 10.6	162 (52.94)	NA	34 (11.11)	48 (15.69)	38.6 ± 3.9	60 (36–144)	59 (19.28)	72 (23.53)
Canpolat (3) [14]	53.5 ± 11.2	172 (47.4)	24.3 ± 3.7	38 (10.5)	33 (9.1)	37.7 ± 4.7	70.8 ± 52.8	0	68 (18.73)
Ciconte (3) [15]	62.7 ± 9.7	18 (28.6)	NA	6 (9.5)	28 (44.4)	47.1 ± 7.9	32.4 ± 34.6	63 (100)	25 (39.68)
Aytemir (2) [16]	54.6 ± 10.5	110 (46)	25.8 ± 6.2	23 (9.7)	19 (8.05)	39.0 ± 5.3	105.6 ± 69.6	48 (20.4)	60 (25.42)
Yorgun [17]	54.5 ± 10.2	69 (47.6)	NA	14 (9.7)	10 (6.9)	38.7 ± 5.4	60 (12–300)	28 (19.3)	26 (17.93)
Evrano [18]	54.6 ± 10.7	36 (60)	NA	5 (8.3)	10 (16.39)	37.4 ± 3.9	36 (24–96)	0	48 (78.69)
Neumann [19]	58 (50–64)	62 (38.1)	27.2 (24.6–30.0)	12 (7.4)	28 (17.18)	52.0 (48–55)	64.9 (24–240)	0	77 (47)

AF — atrial fibrillation; BMI — body mass index; CAD — coronary artery disease; ERAF — early recurrence of atrial fibrillation; LAD — left atrial diameter; LRAF — late recurrence of atrial fibrillation; NA — not available

Table 2. Characteristics of studies included in the meta-analysis

First author/ /years	Location (period) [years]	Total patients	Study design	Cryoballoon type	Endpoint	Follow-up [months]	Population	Independent predictors	HR for AF Recurrence (95% CI)
Mignai [4] 2015	Belgium (2012–2015)	331	Retrospective	28 mm CB-advance	LRAF	13.0 ± 4.3	PAF	ERAF	6.79 (3.52–10.14)
Irfan [5] 2015	Belgium (2012–2014)	393	Retrospective	28 mm CB-advance	LRAF	12.2 ± 3.8	AF	Persistent AF	10.88 (5.72–20.01)
Koektuerk [6] 2015	Germany (2012–2014)	100	Prospective	28 mm CB-advance	LRAF	10.6 ± 6.3	Persistent AF	ERAF	3.83 (1.91–7.68)
Canpolat (1) [7] 2015	Turkey (2010–2011)	41	Prospective	28 mm CB	LRAF	18 (12–20)	PAF	ERAF	1.644 (1.163–2.325)
Boho [8] 2015	Slovakia (2008–2014)	205	Retrospective	23/28 mm CB	LRAF	34 (6–69)	AF	Type of AF	1.97 (1.24–3.13)
Canpolat (2) [9] 2015	Turkey (2010–2013)	402	Prospective	28 mm CB	LRAF	20.6 ± 6.0	AF	AF duration	1.11 (1.08–1.15)
								LAD	1.05 (1.01–1.09)
								ERAF	4.22 (2.20–8.09)
Cicconte (1) [10] 2015	Belgium (2012–2013)	50	Case-control study	28 mm CB-advance	LRAF	12	Persistent AF	LAD	1.03 (0.98–1.08)
								ERAF	2.58 (1.15–5.80)
Cicconte (2) [11] 2014	Belgium (NA)	143	Prospective	28 mm CB-advance	LRAF	12.1 ± 4.4	AF	AF duration	1.31 (1.05–1.63)
								ERAF	18.69 (9.53–36.69)
Gurses [12] 2014	Turkey (2010–2013)	299	Prospective	28 mm CB-advance	LRAF	24 (6–44)	AF	AF duration	1.01 (1.01–1.02)
								LAD	3.09 (1.81–5.27)
								AF duration	1.04 (1.01–1.07)
Aytemir (1) [13] 2014	Turkey (2010–2013)	306	Prospective	28 mm CB-advance	LRAF	22 (13–34)	AF	ERAF	6.39 (3.41–11.97)
								LAD	3.072 (1.646–5.732)
Canpolat (3) [14] 2014	Turkey (NA)	363	Prospective	28 mm CB	LRAF	19.2 ± 6.1	PAF	ERAF	1.906 (1.103–3.291)
								AF duration	1.11 (1.04–1.19)
								ERAF	4.34 (1.9–9.95)
Cicconte (3) [15] 2014	Belgium (2012–2013)	63	Prospective	28 mm CB-advance	LRAF	12	Persistent AF	AF duration	1.31 (1.06–1.62)
								ERAF	2.43 (1.03–5.75)
Aytemir (2) [16] 2013	Turkey (2010–2013)	236	Prospective	28 mm CB	LRAF	18 (6–27)	AF	Persistent	1.26 (1.12–2.56)
								AF duration	1.42 (1.18–2.61)
								LAD	2.42 (1.64–5.88)
Yorgun [17] 2013	Turkey (2010–2012)	145	Prospective	28 mm CB	LRAF	17 (4–27)	AF	ERAF	4.88 (2.86–35.6)
								Persistent AF	1.74 (1.28–2.92)
								LAD	1.17 (1.09–1.27)
Evranos [18] 2013	Turkey (NA)	61	Prospective	28 mm CB	LRAF	10 (8–12)	PAF	ERAF	60 (18.61–417.86)
Neumann [19] 2013	Germany (2005–2007)	163	Prospective	Double walled CB	LRAF	60	PAF	ERAF	3.12 (2.26–5.66)
								LAD	2.11 (1.34–3.31)

AF — atrial fibrillation; CB — cryoballoon ablation; CI — confidence interval; HR — hazard ratio; ERAF — early recurrence of atrial fibrillation; LAD — left atrial diameter; LRAF — late recurrence of atrial fibrillation; PAF — paroxysmal atrial fibrillation

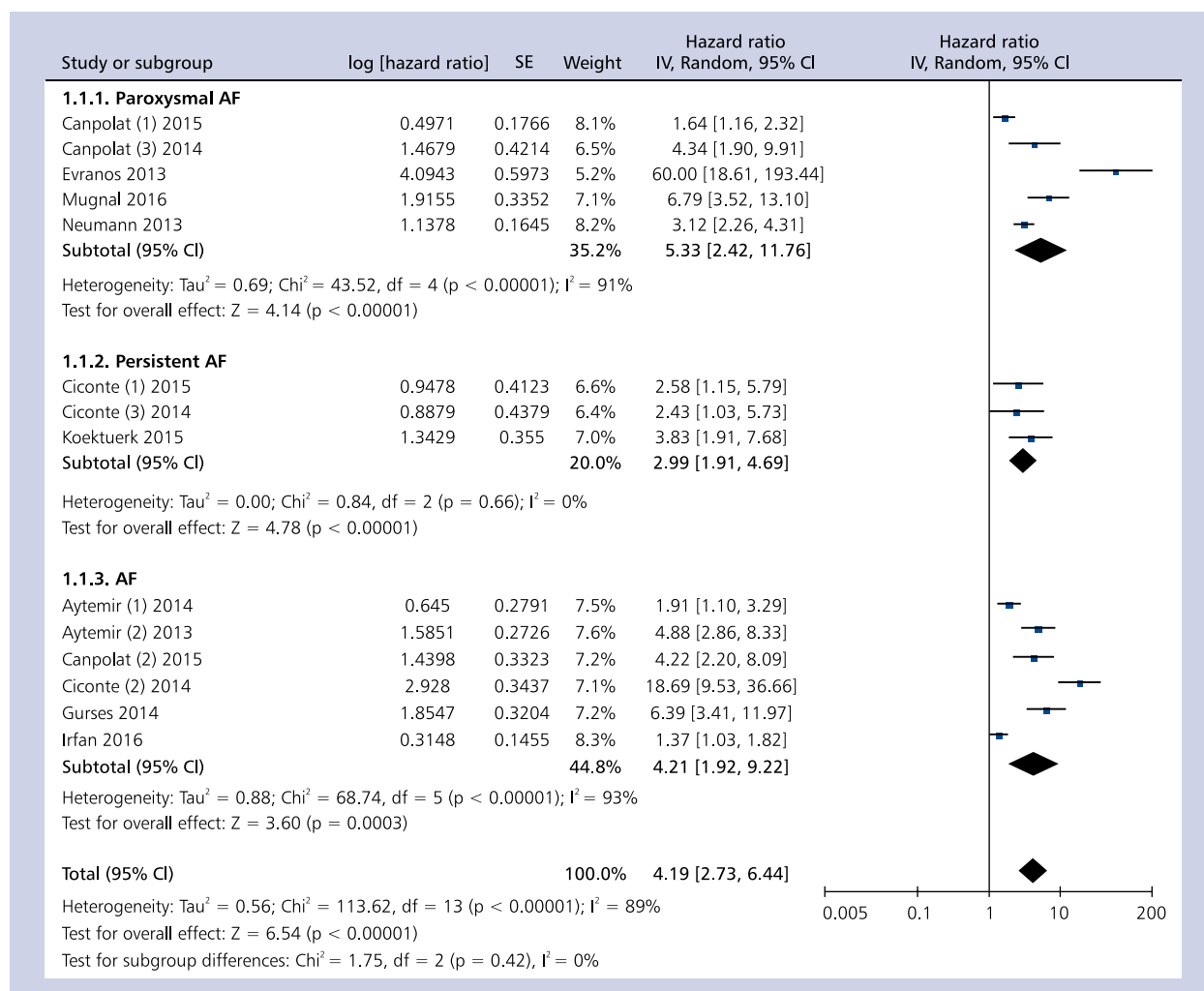


Figure 2. Early recurrence of atrial fibrillation (AF) and late recurrence of AF; CI — confidence interval; SE — standard error

(HR 4.19; 95% CI 2.73–6.44; $p < 0.00001$) with substantial heterogeneity ($p < 0.00001$, $I^2 = 89\%$). For either paroxysmal or persistent AF patients, ERAF could effectively predict the LRAF. Figures 3 and 4 show the results from the random-effects model combining the HR of increased LAD and AF duration. Overall, compared with the control group, patients with either LAD or AF duration experienced a moderate increased risk for developing LRAF with substantial heterogeneity. Also, receiver operating characteristic curves showed that patients with LAD of 37.5 mm and AF duration of 5.5 years could be regarded as having dangerous stages [16].

Figure 5 shows the results from the random-effects model combining the HR of persistent AF. Overall, compared with the control group, patients with persistent AF experienced a significantly increased risk for developing LRAF (HR 2.44; 95% CI 1.30–4.58; $p < 0.006$), with substantial heterogeneity ($p < 0.00001$, $I^2 = 93\%$).

Figure 6 shows the results from the random-effects model combining the HR of CB-advance. A total of eight studies

were included, and only patients with ERAF experienced a significantly increased risk for developing LRAF (HR 4.53; 95% CI 2.47–8.33; $p < 0.01$), with substantial heterogeneity ($p < 0.01$, $I^2 = 82\%$).

Sensitivity analyses

Sensitivity analyses were conducted to explore the potential sources of heterogeneity in the association between each of the risk factors and LRAF and to examine the influence of various exclusion criteria on the overall risk estimate. After excluding the four studies [7, 10, 15, 18] that had the fewest enrolled patients, the analysis did not find a significant influence on heterogeneity across studies or overall results (HR 4.20; 95% CI 2.59–6.79; $p < 0.00001$), ($p < 0.00001$, $I^2 = 88\%$). After excluding the four studies [4, 5, 8, 10] that included studies without prospective studies, the analysis was only slightly changed in terms of the overall risk (HR: 4.69; 95% CI 2.91–7.58; $p < 0.00001$), and no evidence of heterogeneity was observed among the remaining studies

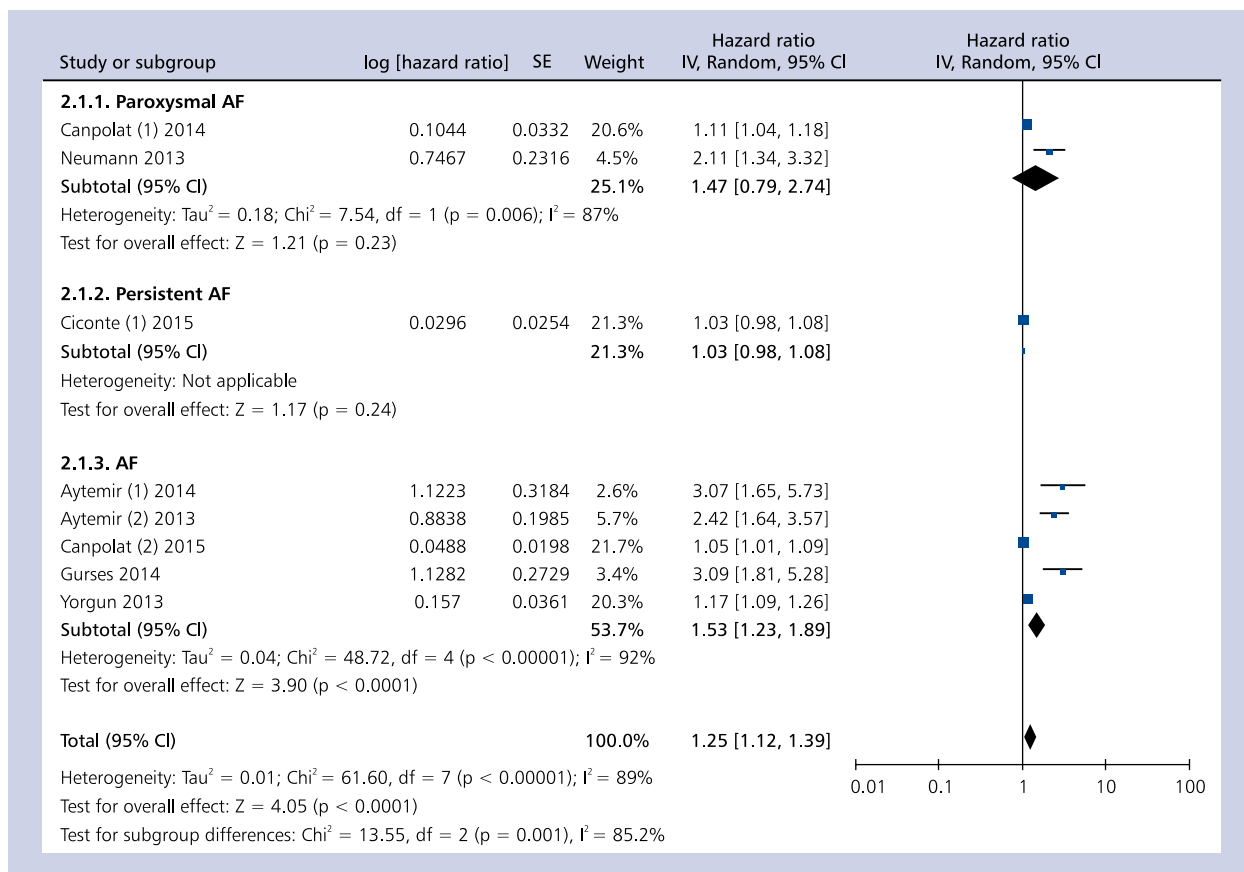


Figure 3. Left atrial diameter and late recurrence of atrial fibrillation (AF); CI — confidence interval; SE — standard error

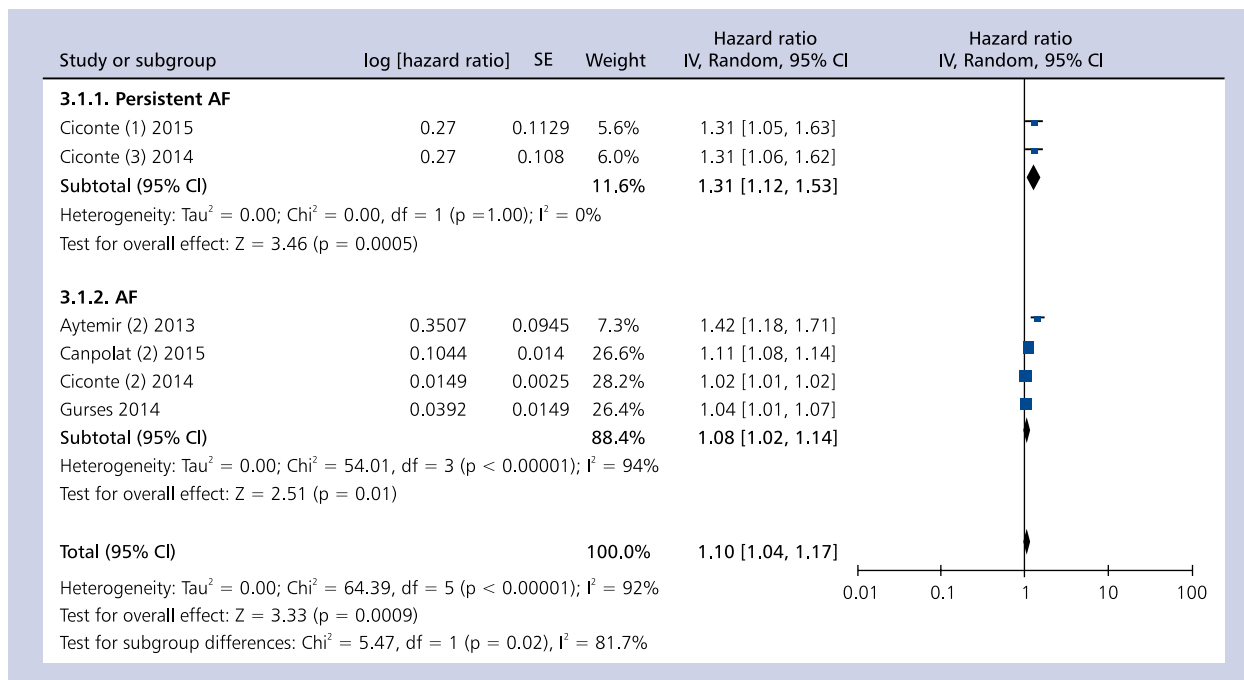


Figure 4. Atrial fibrillation (AF) duration and late recurrence of AF; CI — confidence interval; SE — standard error

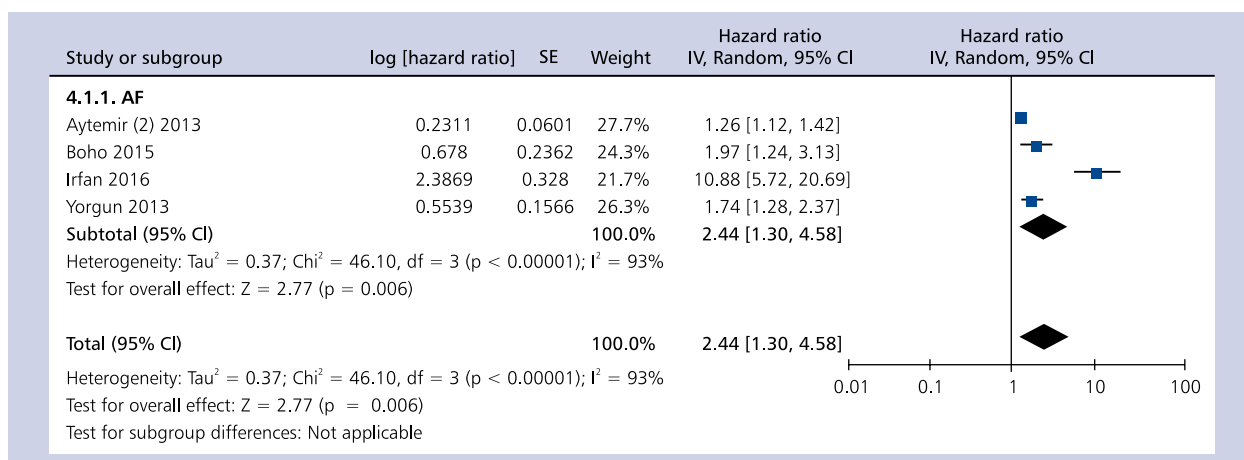


Figure 5. Persistent atrial fibrillation (AF) and late recurrence of AF; CI — confidence interval; SE — standard error

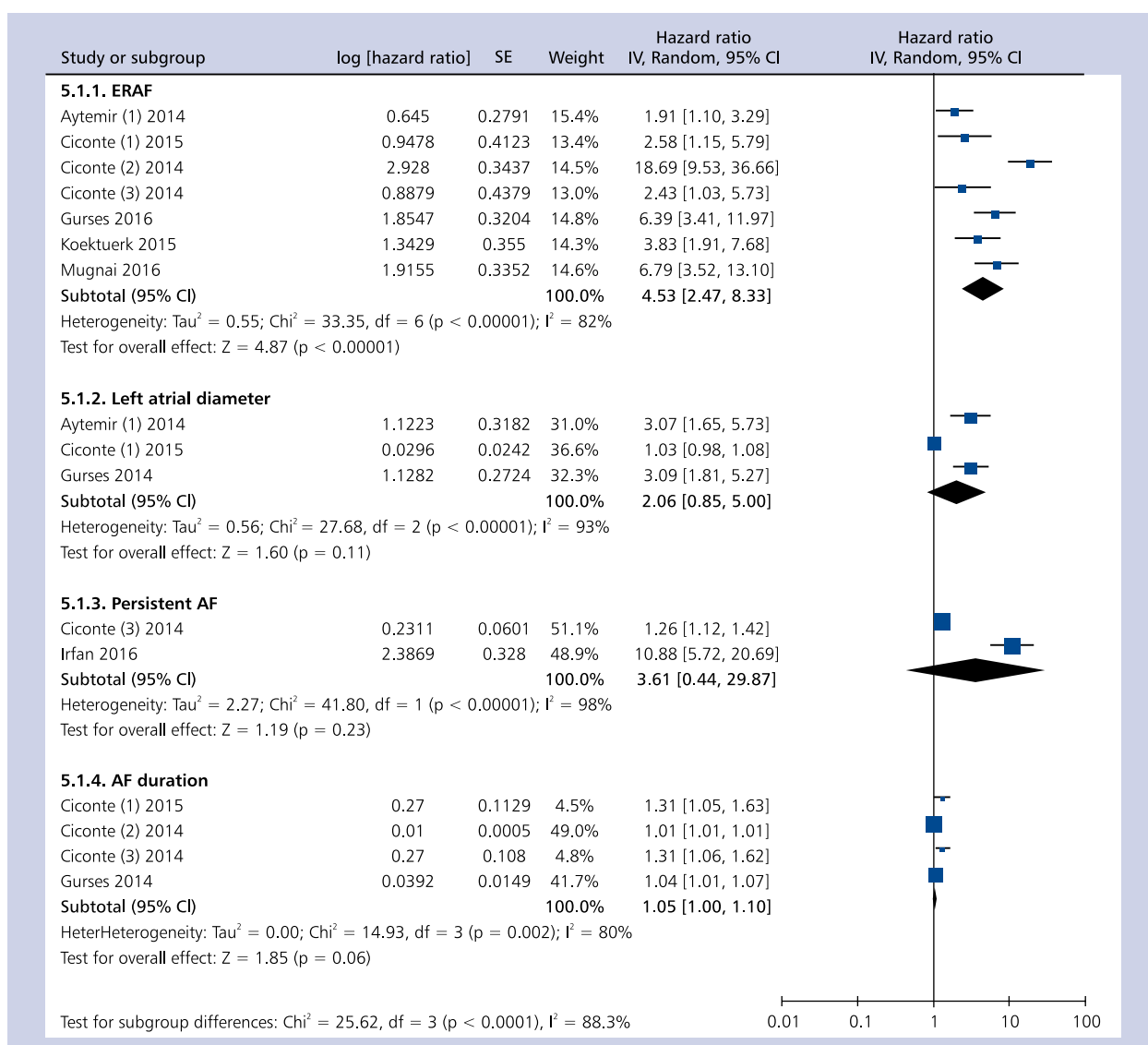


Figure 6. Predictors of late recurrence of atrial fibrillation (AF) in cryoballoon-advance; CI — confidence interval; SE — standard error; ERAF — early recurrence of atrial fibrillation

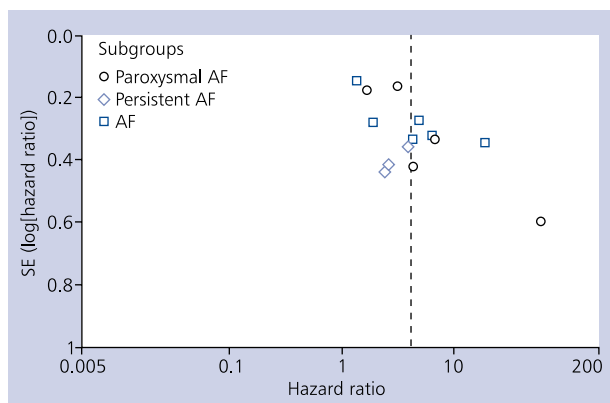


Figure 7. Funnel plot of early atrial fibrillation (AF) recurrence

($p < 0.00001$, $I^2 = 87\%$). The further exclusion of any single study did not markedly alter the overall combined HR.

Publication bias

Figure 7 shows a funnel plot of the HR of the ERAF in the all patients. Studies were not distributed within the 95% CI area. This suggests significant publication bias.

DISCUSSION

It is particularly important to screen for groups with a high risk of LRAF after CB ablation. Using 16 included studies, we defined the ERAF in the “blank period”, left atrial enlargement, a longer duration of pre-ablation AF, and persistent AF as independent risk factors for LRAF (4.19, 1.25, 1.10, and 2.44 times the risk compared to the control group, respectively).

Currently, PVI with radiofrequency current catheter ablation is a safe and effective method for treating AF and can effectively reduce or eliminate the burden of AF [20]. CB technology offers the possibility of PVI with a single energy application, so it has been increasingly used as an alternative to point-by-point RF current ablation in patients with AF. Aytemir et al. [13] showed that freedom from AF was achieved in 68.53% of patients undergoing PVI with CB, with a median 30-month follow-up, and in 90.83% of patients with CB-advance, with a median 10-month follow-up, when the “blinking period” was considered. As shown in our paper, ERAF was the only risk factor for LRAF in AF patients with CB-advance because the risk factors of increased LAD, persistent AF, and long AF duration were not statistically significant. Although the report was limited by the number of included studies, the results agree with the low event-free survival rate of CB-advance. Compared with CB, CB-advance has been redesigned for use in an injection system, with the aim of distributing the refrigerant homogeneously to the frontal balloon surface. Notably, the distal pole and the more distally positioned injection ports have been doubled with CB-advance. These technological improvements have been proven to achieve significantly higher success rates and fewer risk factors when using the CB-advance. Therefore, Aytemir et al. [13] showed that

using the second generation of CB is an independent protective factor for reducing LRAF.

The definite mechanism between the risk factors and LRAF is not clear but may be the result of a combined effect. LRAF is mostly associated with the reconnection and re-excitation of the cardiac proarrhythmic structure. Similar to our research, many studies have found that patients with early recurrence could have an increased risk of late recurrence. Using antiarrhythmic drugs immediately after ablation can reduce early recurrence but cannot prevent late recurrence after three months [6, 7]. Therefore, many studies have hypothesised that the inflammatory response following cell damage caused by CB increases the susceptibility to arrhythmias. It may also change the autonomic nervous system by increasing sympathetic activation and reducing the vagus nerve for remodelling the atrial substrate. Taken together, these factors suggest a premise for late recurrence. Studies have shown that immediate early recurrence after ablation will gradually return to normal within three months, but early recurrence within 1.5 months after ablation is significantly associated with LRAF. Many studies have demonstrated that pulmonary vein reconnection is a major cause of LRAF. Comparing CB with CB-advance, early relapse can be a good predictor of late recurrence due to the more stable and uniform injury by CB-advance. Based on the above features, Mugnai et al. [4] suggested that the occurrence of atrial arrhythmia within 1.5 months after ablation is more likely to cause late relapse. For persistent AF patients, the one-year ablation success rate of CB-advance was 60% [21], indicating moderate outcomes despite a lower success rate compared to paroxysmal AF. The high recurrence of persistent AF was based not only on pulmonary vein reconnection but also on the continuous and long-term maintenance of AF and other non-PVI factors in the left atrium. This could explain why persistent AF may be an independent risk factor for late recurrence.

Many studies also show that increased LAD is an important predictor of the recurrence of AF after PVI. The predictive ability of LAD is associated with the remodelling of the atrial structure. The larger atrium facilitates the reconnection of the pulmonary vein and is not conducive to performing a complete ablation of the complex atrial structure [22]. The PVI is mainly to eliminate the ectopic pacemaker for reverse electrical remodelling and is less powerful to terminate or reverse structural remodelling. Electrical remodelling and structural remodelling are the main mechanisms of AF, and the burden of AF will not only deteriorate the remodelling but also change it to persistent AF. Therefore, some studies have suggested that for the increased LAD and long duration of AF, early intervention and upstream treatment after PVI can effectively relieve or prevent late recurrence [19]. The “dangerous” size of the LAD is different between patients and measurement methods. There is no uniform standard, but studies have shown that a size larger than 4.5 cm is a critical point [21]. The inflammation, as another important mecha-

nism of atrial structural remodelling, can lead to myocardial necrosis and interstitial fibrosis. However, the limited number of studies and wide range of markers make it underpowered to be used as a predictor; thus, more studies are required.

Limitations of the study

This study has some limitations that cannot be ignored. First, the heterogeneity of each study was significant. Although AF type was analysed as a subgroup, heterogeneity still existed. The patients with paroxysmal AF and persistent AF, who were not matched, may be another source of heterogeneity, so more studies are needed. Second, the funnel plot showed publication bias in this study. Most risk factors were examined only once in many of the articles. These articles were removed for lacking repeatability, which could be the main reason for bias. Third, the follow-up period was different in each study, ranging from 10 months to 60 months, which could be another source of heterogeneity. Fourth, studies varied in the quality of electrocardiography monitoring of the patients after PVI. Some studies implanted loop recorders, and others provided seven-day Holter monitoring only.

CONCLUSIONS

This meta-analysis suggests that early recurrence of AF in the “blinking period”, increased left atrial size, long duration of AF before ablation, and persistent AF are independent predictors for late recurrence of AF after CB ablation.

Conflict of interest: none declared

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Cite this article as: Quan D, Huang H, Kong B, et al. Predictors of late atrial fibrillation recurrence after cryoballoon-based pulmonary vein isolation: a meta-analysis. *Kardiol Pol*. 2017; 75(4): 376–385, doi: [10.5603/KPa2016.0186](https://doi.org/10.5603/KPa2016.0186).

Czynniki predykcyjne późnego nawrotu migotania przedsionków po izolacji żył płucnych metodą krioablacji balonowej: metaanaliza

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Streszczenie

Wstęp: Częstość nawrotów migotania przedsionków (AF) po krioablacji balonowej u chorych z AF opornym na farmakoterapię jest bardzo duża. Istnieją różne czynniki predykcyjne późnego nawrotu AF.

Cel: Celem badania była ocena czynników ryzyka umożliwiających skuteczne prognozowanie późnych nawrotów AF po izolacji żył płucnych metodą krioablacji balonowej.

Metody: W okresie od 1 stycznia 2013 r. do 1 sierpnia 2016 r. przeszukano bazy danych PubMed oraz Web of Science i wybrano badania spełniające określone wcześniej kryteria. Przejrzano także piśmiennictwo wyszukanych artykułów. Dwaj autorzy niezależnie uzyskali informacje na temat projektów badań. Moc statystyczną i zależności między różnymi czynnikami ryzyka a późnym nawrotem AF oceniano za pomocą skorygowanego współczynnika hazardu.

Wyniki: Do metaanalizy włączono 16 prac, które spełniły określone kryteria. Współczynniki hazardu w stosunku do grupy referencyjnej wynosiły: dla późnego nawrotu AF u osób z wczesnym nawrotem AF — 4,19 (95% CI 2,73–6,44; $p < 0,00001$); dla zwiększonego wymiaru lewego przedsionka — 1,25 (95% CI 1,12–1,3; $p < 0,0001$); dla długiego czasu trwania AF przed ablacją — 1,10 (95% CI 1,04–1,17; $p < 0,0009$); dla przetrwałego AF — 2,44 (95% CI 1,30–4,58; $p < 0,006$). Jednak występowało istotne zróżnicowanie każdego ze wskaźników, a ponadto zaobserwowano nieznaczny błąd publikacji (*publication bias*).

Wnioski: Wyniki niniejszego badania wskazują, że wczesny nawrót w okresie wygaszania, zwiększony wymiar lewego przedsionka, długi czas trwania AF przed ablacją oraz przetrwałe AF są niezależnymi czynnikami predykcyjnymi późnego nawrotu po krioablacji balonowej.

Słowa kluczowe: krioablacja balonowa, migotanie przedsionków, późny nawrót, czynniki predykcyjne

Kardiologia 2017; 75, 4: 376–385

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Praca wpłynęła: 04.05.2016 r.

Zaakceptowana do druku: 29.11.2016 r.

Data publikacji AoP: 27.12.2016 r.