Atrial fibrillation ablation in Athletes vs. non-Athletes: 5-year experience of a single Italian third-level center.

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Abstract

Introduction. Few data exist about effectiveness of atrial fibrillation (AF) catheter ablation (CA) in athletes and feasibility of resuming vigorous exercise afterwards. Aims of our study were to analyze the efficacy and safety of AF CA in athletes, to compare AF CA outcomes in athletes vs Non-Athletes (NA) and to evaluate the feasibility of resuming vigorous exercise. We additionally analyze the outcome of patients that underwent concomitant cavo-tricuspid isthmus (CTI) CA. Methods and results. From January 2015 to October 2019, 38 athletes were retrospectively matched with 38 NA that underwent first time AF CA. After a median follow-up of 787 days, 62.5% of athletes were free from recurrences after one CA procedure and mostly without antiarrhythmic drugs (87%). Seven athletes underwent a redo procedure and all of them were then free of recurrences with an overall freedom from recurrences of 84%. No major complications were observed. After the first year of follow-up, athletes had a 48% reduced risk of recurrences than NA [adjusted hazard ratio (HR) on antiarrhythmic drugs, LA volume and AF subtype, HR 0.52]. Athletes that underwent also CTI ablation showed a positive trend in terms of freedom from recurrences (50% vs 21%). Most (72%) of the athletes resumed vigorous exercise after at least 3 months from the CA. Conclusion. AF CA is a safe and efficient therapeutic option in athletes and it should be considered instead of drugs to early resume competitive sport activity. Concomitant CTI ablation may have a favorable role.

Introduction

Atrial fibrillation (AF) is the most common cardiac arrhythmia in athletes[1] and the interaction between sport activity and AF is now widely accepted, especially in master athletes who practice long-term endurance sport. Moreover, an association between physical activity and common atrial flutter (AFL)[2] has been described. The mechanism is not fully understood and it is presumed to be multifactorial. A specific trigger (atrial ectopy, sports supplements and illicit drug use) in the presence of a suitable substrate (genetic predisposition, cardiac remodeling with atrium dilation, inflammation and fibrosis) and a modulator (autonomic activation, electrolyte abnormalities, acid reflux disease) is the foundation in onset and maintenance of AF in athletes. Lone AFL seems to be a right-sided expression of the same pro-arrhythmic changes that lead to AF in the left atrium.

Effective treatment of symptomatic AF is mandatory for sport continuation both for European and Italian pre-participation protocols. However, the management of AF in athletes is challenging. Reduction of training volume and intensity may be effective, but in clinical practice most athletes prefer to continue sport at the same level as before. Rate-control strategy of the episodes is difficult to achieve in athletes since beta-blockers are poorly tolerated and even prohibited in some competitive sport. Moreover, pharmacological rhythm-

control strategy is poorly tolerated because of sinus bradycardia and/or arterial hypotension. Long term antiarrhythmic drug therapy does not represent the first choice in a young and otherwise healthy population. Therefore, catheter ablation (CA) should be early considered in athletes.

Furthermore, any form of anticoagulation can be a challenge due to increased risk of bleeding with sport activities and it is a contraindication to all sports with intrinsic risk or interpersonal contact. There are no data regarding the safety of novel anticoagulants in athletes with AF. Given the increasing age of athletes, it is not rare to achieve a CHA_2DS_2-VASc score [?] 1 that may indicate the need for stroke prevention, especially when the arrhythmic burden is high (class IA for score [?] 2, class IIaB for score of 1). Efficient AF control through CA could also permit to stop anticoagulant treatment in most athletes.

AF ablation is therefore an effective and safe therapeutic option and recent international guidelines strongly recommend CA in paroxysmal AF patient in whom at least one AAD has failed or is not well tolerated (class I) and recommend AF ablation as first-line therapy in selected patients (class IIa)[3,4]. All guidelines emphasize the importance of high annual procedure volumes for operators and sites.

However, few data exist about the effectiveness of AF CA in athletes and feasibility of resuming vigorous exercise afterwards.

Aims of our study were to analyze the efficacy and safety of AF CA in athletes, to compare AF CA outcomes in athletes vs Non-Athletes (NA) and to evaluate the feasibility of resuming vigorous exercise. We additionally analyze the outcome of patients that underwent concomitant AFL CA.

Methods

Study population

We report a retrospective registry of athletes referred to our Sports Cardiology Center (Centro Cardiologico Monzino IRCCS) for AF CA in the last five years. All athletes were previously declared non-eligible to competitive sport at pre-participation screening because of recurrences of AF or evidence of persistent asymptomatic AF. Sedentary patients without any structural heart disease were matched with athletes based on age and sex.

All patients underwent a complete clinical assessment including ECG, echocardiogram and thyroid function test. A full medical history and a query for drug use (especially performance-enhancing drugs) were included. Additional diagnostic tests were performed if needed.

Catheter ablation

Procedural methods, catheter selection, and post-procedural medication management followed general practice. All patients underwent isolation of the pulmonary veins (PVI) either by radiofrequency ablation or cryoablation. Cavo-tricuspid isthmus ablation (CTI) was performed discretionally regardless previous documentation of typical AFL.

Clinical Follow up and outcomes

Clinical follow-up of patients was performed through periodic ambulatory clinical visits with ECG, Holter monitoring and ergometric stress test before resuming sport activity. Patients were asked in detail about clinical events occurring during the period of follow-up and documentation of the events was carefully checked. Recurrences were defined as reactivation of symptoms and/or any documentation of AF lasting more than 30 sec. At the end of the follow-up all patients were asked about resuming sport.

Statistical analysis

To minimize between-group differences at baseline, 38 athletes that underwent first time CA for paroxysmal AF in our Institution and Non-Athletes were matched by sex, age ($\pm$ 5 y) and year of CA ($\pm$ 2 y). Continuous variables are presented as mean $\pm$ standard deviation, and they were compared using t test for independent samples. Non-normally distributed variables are presented as median and interquartile ranges, and they were

compared with the Wilcoxon rank sum test. Categorical data were compared using $\chi 2$ test or Fisher's exact test, as appropriate

The association of AF recurrences in the two groups were tested by multivariate Cox regression model and Kaplan Meier excluding any episode occurred in the first three months (blanking period). Log-rank tests were used to compare strata. All tests were 2-tailed, and P<0.05 was required for statistical significance. All analyses were performed using SAS version 9.4 (SAS Institute, Cary, NC).

Results

Population characteristics

The main clinical characteristics of patients are shown in **Table 1** . From January 2015 to October 2019, 38 athletes underwent first time CA for paroxysmal atrial fibrillation in our Institution and were matched to 38 NA. Athletes and NA were mostly males (95%) with a mean age of 48±13 years. Non-athletes had significant higher BMI than athletes [respectively, 27.8 (26.3-29.8) kg/m^2 vs. 24.2 (22.9-26) kg/m^2, P < 0.0001] and suffered more often from dyslipidemia (19% vs. 3%, P = 0.0247) and hypertension (32% vs. 5%, P = 0.003) and therefore CHA_2DS_2-VASc score was lower in athletes (P = 0.0187). In NA AF was more often early-persistent (70% vs. 21%, P = 0.076) than paroxysmal (27% vs. 76%, P < 0.0001) and they were therefore more often in anticoagulant therapy (86% vs. 42%, P < 0.0001) but less often in antiarrhythmic drugs (41% vs. 68%, P = 0.010). LA volume was significantly higher in NA (43±12 vs. 36±11ml/m2, P = 0.0295).

Distribution between type of sport is illustrated in **Figure 1** .

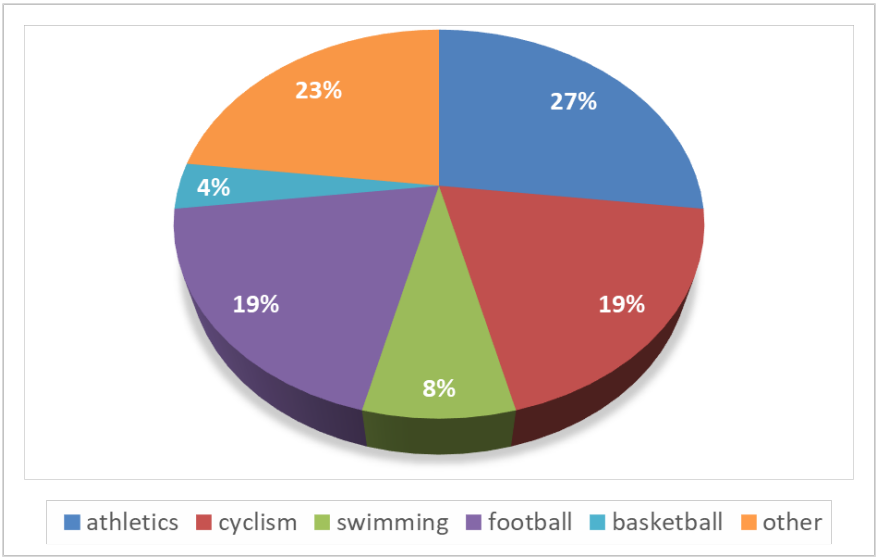
Table 1.

	Athletes (n=38)	**Non-athletes (n=38)**	**P-value**
Age at CA	48±13	50±10	0.3908
Male	36 (95)	36 (97)	0.9847
Hypertension	2 (5)	12 (32)	0.0030
Diabetes mellitus	0 (0)	1 (3)	0.3140
Dyslipidemia	1 (3)	7 (19)	0.0247
BMI (kg/m^2)	24.2 (22.9-26)	27.8 (26.3-29.8)	**<.0001**
CHA_2DS_2-VASc score	0 (0-0)	0 (0-1)	0.0187
EHRA symptoms score	2 (1-2)	1 (1-2)	0.3305
AAD	26 (68)	15 (41)	0.0101
Class Ic at CA	18 (69)	11 (73)	0.1166
Class II at CA	7 (27)	1 (7)	0.0247
Class III at CA	4 (15)	3 (20)	0.7189
Anticoagulant at CA	16 (42)	32 (86)	<.0001
Acenocumarol/warfarin	3 (19)	10 (31)	0.0286
Direct anticoagulants	13 (81)	22 (69)	0.0284
AF subtype			
Paroxysmal	29 (76)	10 (27)	<.0001
Early-persistent	8 (21)	26 (70)	0.0760
Long-persistent	1 (3)	1 (3)	1
AF diagnosis prior CA (years)	2 (1-4)	2 (1-4,5)	0.8097
Echocardiogram			
LVEF (%)	61±5	56±9	0.0133
LA Vol (ml/m^2)	36±11	43±12	0.0295

Data are presented as mean ± standard deviation, n (%), or median (interquartile range).

AAD, antiarrhythmic drugs; AF, atrial fibrillation; BMI, body mass index; CA, catheter ablation; EHRA, European Heart Rhythm Association; LA, left atrium; LVEF, left ventricular ejection fraction.

Figure 1.



Distribution between type of sport.

Procedural characteristics

The main procedural characteristics are shown in **Table 2** . Athletes were treated almost 1:1 with cryo and RF ablation, while in NA RF was chosen in most of cases [RF 21 (55%) vs 35 (92%), P=0.00057; cryo 17 (45%) vs 3 (8%), P = 0.00012]. LA target different from pulmonary veins was ablated only in NA [8 (21%) vs 0, P = 0.0129], while CTI was performed significantly more often in athletes [16 (42%) vs 5 (13%), P = 0.0047].

Table 2.

	Athletes (n=38)	**Non-athletes (n=38)**	**P-value**
1st CA procedure			
PVI	38 (100)	38 (100)	1
CTI	16 (42)	5 (13)	0.0047
Other LA target	0 (0)	8 (21)	0.0129
SAE	0 (0)	0 (0)	1
RF	21 (55)	35 (92)	0.00057
Cryo	17 (45)	3 (8)	0.00012
Redo CA procedure	5 (13)	6 (16)	0.74440
Redo before 1 year	1 (20)	2 (33%)	0.55579
Redo after 1 year	4 (80)	4 (77%)	1

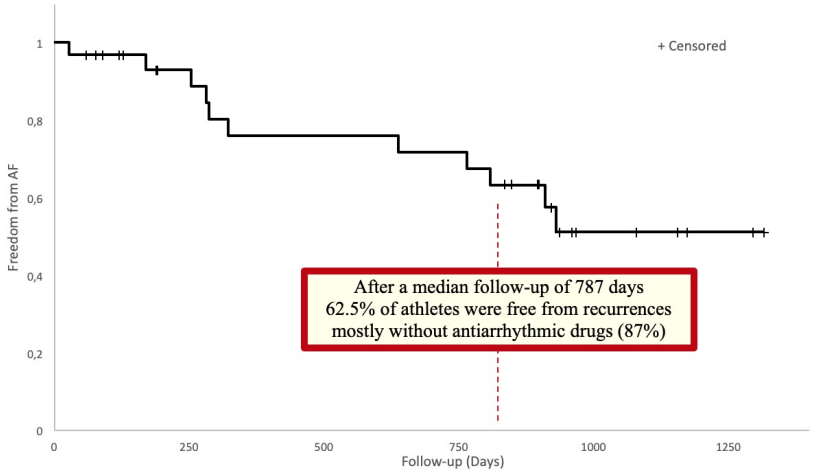
Data are presented as n (%).

CA, catheter ablation; CTI, cavo-tricuspid isthmus; LA, left atrium; PVI: pulmonary vein isolation; RF, radiofrequency; SAE, serious adverse event.

Outcomes

Outcomes in athletes. After a median follow-up of 787 days, 62.5% of athletes were free from recurrences after one CA procedure and mostly without antiarrhythmic drugs (87%). Seven athletes underwent a redo procedure and all of them were then free of recurrences with an overall freedom from recurrences of 84% (**Figure 2**). No major complication was observed. Athletes practicing endurance sports showed a negative trend in terms of recurrences (p = ns).

Figure 2.

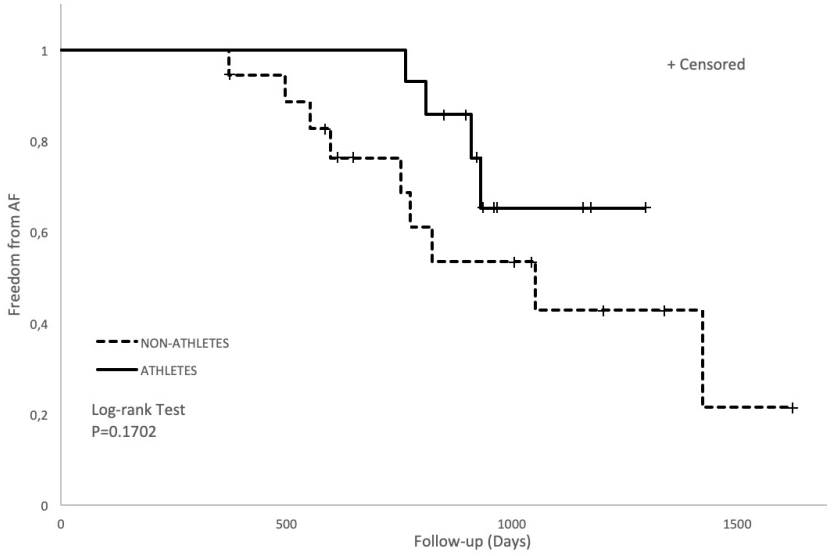


Kaplan-Meyer of AF recurrences in athletes.

Most (72%) of the athletes resumed vigorous exercise after at least 3 months from the CA, successfully passed preparticipation screening and could be eligible again for competitive sport activities in agreement with Italian sport protocols.

Ouctomes in athletes vs non-athletes. After the first year of follow-up, athletes had a 48% reduced risk of recurrences than NA [adjusted hazard ratio (HR) on antiarrhythmic drugs, LA volume and AF subtype, HR 0.52]. These data were confirmed and more significant in an age-related analysis in which young patients (< 49 years old) were compared to old patients (> 49 years old) of both groups. Young athletes had a risk of AF recurrences 4 times lower (HR 3.98) than young NA, while elderly athletes had a 46% reduced risk of AF recurrences (HR 1.46) than elderly NA. These differences were not statistically significant due to low sample size, but showed a positive trend in athletes vs NA (**Figure 3**).

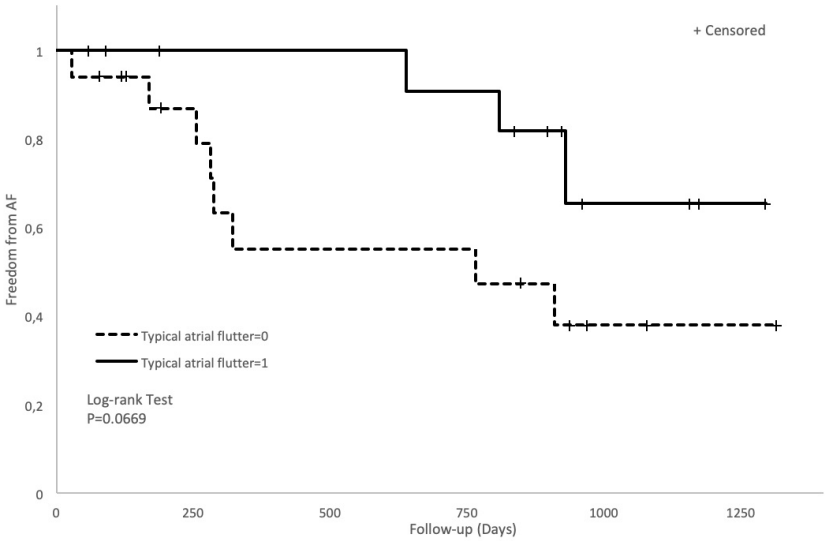
Figure 3.



Kaplan-Meyer of AF recurrences in athletes vs non-athletes. Adjusted on antiarrhythmic drugs, LA volume and AF subtype.

Outcomes with concomitant CTI ablation. CTI ablation was performed in 16 athletes (43%). Athletes that underwent also CTI ablation showed a positive trend in terms of freedom from recurrences (50% recurrences in AF CA only vs 21% in CTI plus AF CA,**Figure 4**). The statistical significance was borderline due to small sampling size (p = 0.06, Kaplan-Meier log-rank 3.3587).

Figure 4.



Kaplan-Meyer of arrhytmia recurrences after AF ablation vs concomitant CTI ablation.

Discussion

The main finding of this study is the higher propensity of athletes population of remaining free from AF recurrences after a single AF ablation procedure compared with Non-athletes population, especially when CTI ablation was associated with PVI. Furthermore, the majority of our athletes population quickly resumed competitive sport activity.

Data from the literature suggest that freedom from AF is between 50-80% in patients with either persistent or paroxysmal AF[5-10]. However, there are few and conflicting long-term data available in athletes and no difference in long-term freedom from AF has been observed between athletes and NA.

In 2008 Furlanello et al. reported in a small population of 20 athletes (mean age 44.4±13 years) 90% freedom from AF at 36.1±12.7 months after PVI[11]. Another study including 182 subjects undergoing PVI reported similar arrhythmia-free survival at one year in the lone AF sport group versus controls (59% vs 48%, p=0.44), and similar rates of procedure related complications (7.1% vs. 4.3%; p=0.45). The frequency of redo PVI procedures was similar between the lone AF sport group and controls (40.5% vs 37.3%, p=0.5)[12]. Koopman et al. studied 94 endurance athletes and reported similar AF recurrence after first PVI procedure[13]: both groups showed similar arrhythmia free survival at 3 years (87 vs. 85%, p=0.88).

More recently, the case-control study by Decroocq et al.[14] showed the same AF recurrences rates at 1-year follow-up after CA between 73 athletes and 73 matched sedentary patients. After 5-year follow-up, AF recurrences rates did not differ statistically between 38 (52%) athletes and 35 (47.9%) NA who recurred. Finally, Mandsager et al.[15] reported no difference in arrhythmia recurrence between athletes and a matched cohort of NA who underwent PVI. Single-procedure freedom from arrhythmia was 75%, 68%, and 33% at 1 year for paroxysmal, persistent, and long-standing persistent AF, respectively. Multiple-procedure freedom from arrhythmia off antiarrhythmic drugs was 86%, 76% and 56% in respective group at the end of follow-up (mean 1.4 ± 0.7 ablation per athletes).

In our study, after a median follow-up of 787 days, 62.5% of athletes were free from recurrences after one CA procedure and mostly without antiarrhythmic drugs (87%), while after a redo procedure the overall freedom from recurrences was 84%. However, in contrast with previous data, our study showed a higher propensity of athletes of remaining free from AF recurrences after a single AF ablation procedure compared with NA population. After the first year of follow-up, athletes had, in fact, a 48% reduced risk of recurrences than NA, especially in an age-related analysis. Young athletes had a risk of AF recurrences 4 times lower than young NA, while elderly athletes had a 46% reduced risk of AF recurrences than elderly NA. These differences were not statistically significant due to low sample size, but showed a positive trend in athletes.

Different reasons may explain a better outcome of CA in athletes compared to NA. First of all, athletes were slimmer than NA and the correlation between BMI and AF is clearly demonstrated[16-18]. Moreover, in NA LA volume was significantly higher and persistent AF significantly more prevalent, suggesting the presence of atrial remodelling and more advanced electric LA disease. It has been demonstrated, in fact, that even small difference in LA volume is an independent predictor of increased odds of AF recurrence[19]. The negative trend showed in endurance athletes may be correlated with atrial remodelling described in this subpopulation of athletes[20]. Endurance training leads to a harmonic enlargement of all four cardiac chambers as an adaptation to exercise conditioning; however, the atrial walls are significantly thinner than the ventricular walls and the higher stress during episodes of training-related volume overload may contribute to progressive LA enlargement and remodelling. Repetitive episodes of atrial stretching and chronic inflammation secondary to excessive endurance training may be contributing factors for atrial fibrosis and AF, especially in aging athletes[21,22].

Furthermore, in our study concomitant CTI ablation in athletes seemed to be associated with an additional positive trend in terms of freedom from recurrences, regardless previous documentation of typical AFL. AFL often precedes or coexists with AF in athletes as a consequence of exercise-induced enlargement of the

atria[23] and it may also be life-threatening during exertion due to 1-to-1 conduction to the ventricles under high sympathetic tone. Our results are in contrast with available data from literature in NA population showing that prophylactic CTI ablation irrespective of the previous documentation of typical AFL is not associated with improvement in recurrence of atrial arrhythmia compared with PVI alone. After the small randomized controlled trial by Pontoppidan et al. in 2009[24], more recently Mesquita et al.[25] compared the outcomes of patients without any previous documentation of typical AFL who underwent PVI alone vs. PVI + prophylactic CTI ablation using a registry dataset of more than 1900 consecutive patients who underwent a first AF CA. CTI ablation remained unassociated with AF-free survival. The same results were obtained by Lee et al. in 2019 in their retrospective study of 139 patients[26] and they were confirmed also by the meta-analysis by Romero et al. in 2020[27]. Ongoing randomized control trials in general population may give further evidence to support or refuse prophylactic CTI ablation. Increased vagal tone and structural atrial changes (i.e. fibrosis) associated with high intensity sport practice may have a causative role in the development of typical AFL in athletes and it may explain our results. However, further data are requested. Recent recommendations for participation in leisure-time physical activity and competitive sports suggest that in an athlete presenting with AFL, there should be a very low threshold to ablate the CTI, given the efficacy and safety of the procedure versus the risk for recurrences during sports. European recommendations even advice that CTI should be ablated prophylactically in athletes with AF who want to engage in intensive exercise, especially when drug treatment is considered or concomitantly with PVI[28].

Lastly, the high success rate of AF CA obtained in our study confirmed the possibility to permanently abolish AF in athletes, offering a unique option for resume competitive sport. Most of our athletes were, in fact, declared eligible to competitive sport activity after at least 3 months from the CA as per Italian sport protocol.

Limitations

The main limitation of the study is an observational, non-randomized, retrospective, low sample size design. The low sample size affected also statistical power and it prevented to analyze if there were any differences in outcome depending on type of sport and time distance between AF diagnosis and CA time. Furthermore, assessment of recrudescence was performed mainly with 24-hour Holter monitoring and asymptomatic AF episodes may have been lost. However, athletes tended to be more often symptomatic than NA and asymptomatic AF should not have significantly affected success rate in athletes. CTI concomitant ablation was left to operator choice and it may have affected final results. Further prospective studies with a larger number of patients are required.

Conclusions

AF catheter ablation is a safe and efficient therapeutic option in athletes and it should be considered instead of drugs to early resume competitive sport activity. Concomitant CTI ablation may have a favorable role in this subset of patients.

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