Atriyum fibrilasyonu tedavisinde kriyobalon tekniği ile pulmoner ven izolasyonu: Tek merkez deneyimi

Pulmonary vein isolation with the cryoballoon technique in the management of atrial fibrillation: a single centre experience

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ÖZET

Amaç: Kriyotermal enerji kullanılarak uygulanan pulmoner ven (PV) izolasyonu tekniği atriyum fibrilasyonu (AF) olan hastaların tedavisinde yakın zamanda kullanıma giren bir yöntemdir. Radyofrekans (RF) ablasyonuna göre işlem süresinde ve ciddi komplikasyon oranında azalma sağladığı düşünülmektedir. Bu çalışmada, kriyobalon tekniği ile AF ablasyonu uyguladığımız hastaların özellikleri ve izlem sonuçları sunuldu.
Çalışma planı: Toplam 236 hastaya (126 erkek, 110 kadıın; yaş ort. 54,6±10,45; dağılım 16-78 yıl) semptomlu AF nedeniyle 28 mm kriyobalon ile PV izolasyonu yapıldı. Hastalarda en az bir antiaritmik ilaç kullanımına karşın başarısız olundu. İşlem sonrası ilk 3 ay kör dönem kabul edildi. Hastalar ortanca 14 (3-24) ay izlendi. İşlem başarısı, komplikasyonlar ve izlem sonuçları güncel Kalp Ritmi Birliği kılavuzundaki tanımlara göre belirlendi.
Bulgular: Akut işlem başarısı (≥3 PV izolasyonu) %99,5 olarak saptandı. Ortalama işlem ve foroskopi süreleri 72.5±5,3 (50-90) dk ve 14±3,5 (12-24) dk idi. Majör komplikasyon 3 hastada (%1,2) gözlendi. Ortanca 14 aylık izlemde AF'siz yaşam paroksismal AF grubunda %80,6, persistan AF grubunda ise %49,2 idi. AF'si tekrarlayan 10 hastaya RF ile AF ablasyonu yapıldı. Çok değişkenli regresyon analizinde sigara kullanımı, beden kütle indeksi, paroksismal olmayan AF tipi, AF süresi (yıl), sol atriyum boyutu ve erken yineleme 3. aydan sonraki yinelemenin öngördürücüleri olarak saptandı.
Sonuç: Bu çalışma Türkiye'de kriyobalon tekniği ile AF ablasyonu deneyimini yansıtan ilk seridir. Tek işlem başarısının özellikle paroksismal AF'li hastalarda istenilen düzeyde olması, komplikasyon oranının oldukça düşük olması, kribalon ile AF ablasyon tedavisinin etkin ve güvenilir olduğunu göstermektedir. Özellikle erken yineleme gelişen hastalar kör dönem sonrası yineleme açısından yakından izlenmelidir.

ABSTRACT

Objectives: Pulmonary vein (PV) isolation with cryothermal energy is a recently introduced technique in patients with atrial fibrillation (AF). It may reduce procedural times and serious complications associated with radiofrequency (RF) ablation. We aimed to present the baseline characteristics and follow-up data of our study population undergoing cryoballoon AF ablation.
Study design: A total of 236 patients (126 males, 110 females; mean age 54.6±10.45; range 16 to 78 years) underwent PV isolation with 28 mm cryoballoon with the indication of symptomatic AF. The treatment of these patients was unsuccessful with at least one previous antiarrhythmic drug. The postprocedural first 3 months was defined as blanking period. Median follow-up time was 14 (3-24) months. Procedural success, complicaitons, and follow-up results were defined according to Heart Rhythm Society guidelines.
Results: Acute procedural success rate (≥3 PV isolation) was 99.5 percent. Mean procedural and fluoroscopy times were 72.5±5.3 (50-90) min and 14±3.5 (12-24) min. Major complications were observed in 3 patients (1.2%). At the median 14 month follow-up, 80.6% of the paroxysmal AF and 49.2% of the persistent AF patients did not experience AF recurrences. RF ablation was performed in 10 patients with recurrences. Smoking, body mass index, non-paroxysmal AF type, AF duration (years), left atrial size, and early recurrence were the predictors of recurrence in multivariate regression analysis.
Conclusion: This study represents the first experience with cryoballoon ablation technique for AF in Turkey The efficacy and safety of cryoballoon AF ablation technique was shown thanks to the acceptable success and low complication rates in paroxysmal AF patients. Particularly, patients who developed early recurrences should be closely followed-up.

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Atrial fibrillation is the most frequently encountered cardiac rhythm disorder.[1] It is the most frequent cause of referrals to the emergency service, and hospitalizations which is associated with decreases in quality of life, functional capacity, cardiac performance, and life span.[2-4] Favourable effects of AF-catheter ablation on quality of life, and functional capacity have been demonstrated. This prcd creates a circular lesion on the pulmonary vein (PV) orifice to enable electrical isolation of triggering foci .[5-7]

Many studies have demonstrated relative success of radiofrequency (RF) catheter ablation over antiarrhytmic drugs in the treatment of symptomatic AF.[8,9] However, incidence of major complications such as thromboembolism, cardiac perforation, and damaged adjacent structures have not decreased as presumed..[4,8-11] Success of RF catheter ablation is extremely dependent on the operator's experience, and also its longer procedural time which all constitute other limitations of the technique. Therefore increasing number of attempts have been directed to develop safer, and more effective PV-isolation technologies with lesser operator dependency

Recently cryothermal ablation technique using balloon catheters (Arctic Front catheters®) whose effectiveness has been demonstrated in preclinical, and clinical studies has been introduced into clinical practice as an alternative AF therapy. This technique creates a scar tissue on left atrium-PV junction so as to provide electrical isolation which abolishes the function of PVs in induction, and maintenance of AFs. Many literature studies have demonstrated that cryoablation method decrease the risk of complications, and procedural times with success rates comparable to those of RF ablation [12,13]

The objective of this study is to provide information about procedural success rates, and postoperative follow-up results in patients who had undergone AF ablation with cryoballoon technique, and determine parametres predicting development of recurrences following blanking period.

PATIENTS AND METHOD

Patients

All patients gave their informed consents before realization of this study with prospective, non-randomized, and observational design The study was organized in compliance with the World Medical Association (WMA) Declaration of Helsinki, and approval for the study protocol was obtained from the local ethics committee.

Abbreviations

AF	*Atrial fibrillation*
ÇKBT	*Çok kesitli bilgisayarlı tomograf*
EHRA	*European Heart Rhythm Association*
PV	*Pulmoner ven*
RF	*Radyofrekans*

A total of 236 patients who consulted to cardiology outpatient clinics between September 2010, and May 2012 with symptomatic paroxysmal or persistent AF despite treatment with at least one antiarrhytmic drug, and scheduled for AF ablation with cryoballoon were enrolled into the study

Patients with moderate-severe valvular disease,left atrial thrombus, thyroid dysfunction, marked left atrial dilatation (left atrial anteroposterior diameter >55mm), coronary artery disease as detected during preprocedural evaluation, pregnants, and those with contraindication to anticoagulant therapy were excluded from the study. From all patients a detailed medical history regarding AF, and AF-related cardiovascular, and other conditions was obtained and also meticulous physical examination was performed at baseline. The complaints of the patients were graded in accordance with European Heart Rhythm Association (EHRA) score system recommended in current guidelines.[14]

Episodes of atrial fibrillation terminating spontaneously within 7 days were defined as paroxysmal AF, and episodes lasting longer than 7 days or those requiring medications or direct current cardioconversion (DCC) were termed as persistent AF.[14]

Preablation evaluation

Before the procedure standard transthoracic echocardiograms, transesophageal echocardiograms were obtained to rule out left atrial thrombus, and for the evaluation of PV multislice computed tomograms (MSCT) of the patients (Figure 1). Anticoagulant therapy of the patients were terminated at least 48-72 hours before initiation of the procedure. When INR dropped below 2, enoxaparine at a dose of 1 mg/kg was started to bridge the time interval, and we proceeded with the procedure when INR was < 1.5. If the patient were using antiarrhytmic drugs, then a time period more than 5 times the half lives of the medications was allowed to pass before starting on the procedure or amiodaron therapy was stopped three months previously.

Ablation procedure

The procedure was performed under conscious sedation provided by administration of midazolam. During the procedure, invasive arterial pressure, and oxygen saturation measurements, and EKG

monitorization were performed. Using Seldinger technique, right femoral vein, and femoral

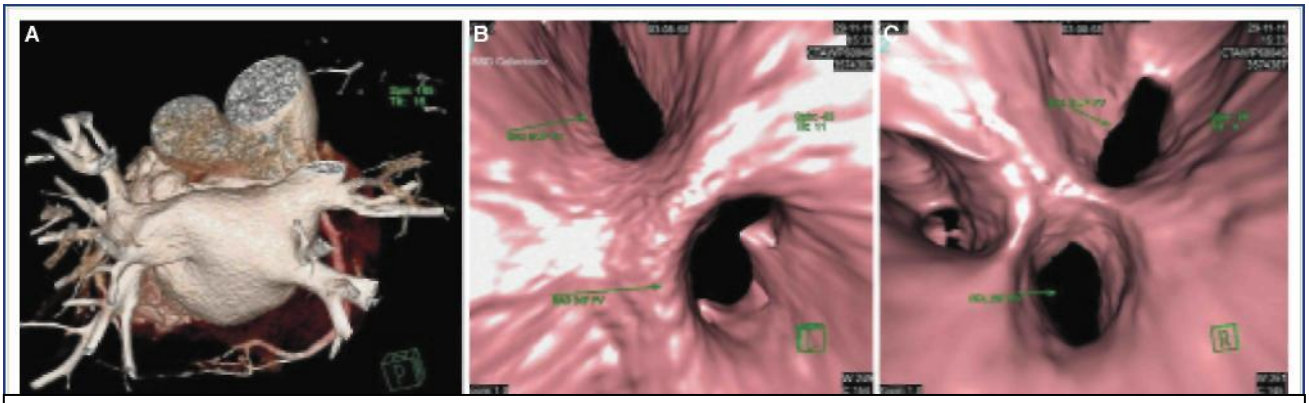


Figure 1. Evaluation of the pulmonary vein anatomy using multislice computed tomography **(A)** 3-D reconstruction **of the l**eft, and the right pulmonary veins as seen through anteroposterior window **(B)** Endoscopic, and 3-D volumetric reconstruction demonstrating right lower, and upper pulmonary veins

In case of need, a 6F steerable decapolar catheter (Dynamic Deca, Bard Electrophysiology, Lowell, MA, USA) was implanted into coronary sinus so as to stimulate atrium/ventricle, and for anatomical reference. This catheter was concurrently advanced into superior vena cava to stimulate phrenic nerve during isolation of the right PV. Transseptal puncture was performed using Brocken-Brough transseptal needle (BRK-1, St. Jude Medical, Minnetonka, MN, USA) under fluoroscopic control. Then, 12 F steerable delivery sheath (outer diameter:15 mm; FlexCath, Cryocath, Montreal, Quebec, Canada) was placed in the left atrium. During the procedure anticoagulation was administered so as to achieve an activated clotting time of 300-350 secs using intravenous unfractionated heparin.

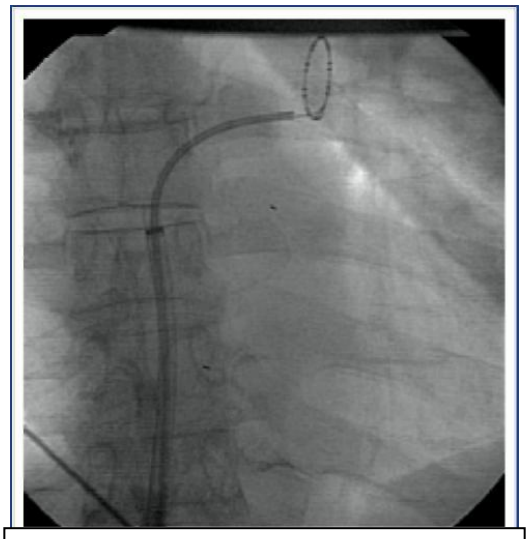


Figure 2 A CT image demonstrating a circular mapping catheter (Lasso) exploring potential foci around the left upper pulmonary vein orifice.

artery/vein punctures were carried on.

Before insertion of a single transseptal sheath, circular mapping catheter (Lasso, Biosense Webster, Inc., Diamond Bar, CA, USA) was passed through to explore PV potentials. To discriminate between PV, and atrial potentials, stimuli were delivered from coronary sinus.PV After detection of PV potentials circular mapping catheter was removed, and a 28-mm cryoballoon catheter (Arctic Front©, Medtronic CryoCath LP, Kirkland, Canada) was passed through this transseptal sheath was directed into PVs with the aid of a guidewire (0.035 inch, 180 cm SuperStiff, St Jude Medical, St. Paul, MN, USA) Transseptal sheath was rapidly, and continually irrigated with heparinized physiologic saline solution at a rate of 3-4 ml/sec.

After access into the targeted vessel with a guidewire, balloon catheter was inflated in the left atrium, and oriented through PV orifice. Then, a contrast agent diluted 50 % with physiologic saline was infused through balloon catheter to determine the patency of PV (Figure 3). After confirmation of the proper position of the catheter with contrast agent injection, cryotherapy was used for five minutes. During ablation of the right PV, decapolar catheter in the coronary sinus was implanted in the superior vena cava to stimulate phrenic nerve for the prevention of paralysis of the phrenic nerve. During the procedure, manual abdominal examination was performed to monitor the severity of the pacing. Decreased abdominal contractions necessitated prompt termination of cryoablation. For each PV, 5-minute- sessions of cryotherapy were instituted for at least 2 times, and following ablation of all PVs, circular mapping catheter was placed in PVs to determine PV isolation. (Figure 4). Ablation of PV potentials, dissociation of PV potential (Figure 5) or blockage of entry were accepted as endpoints of the procedure.

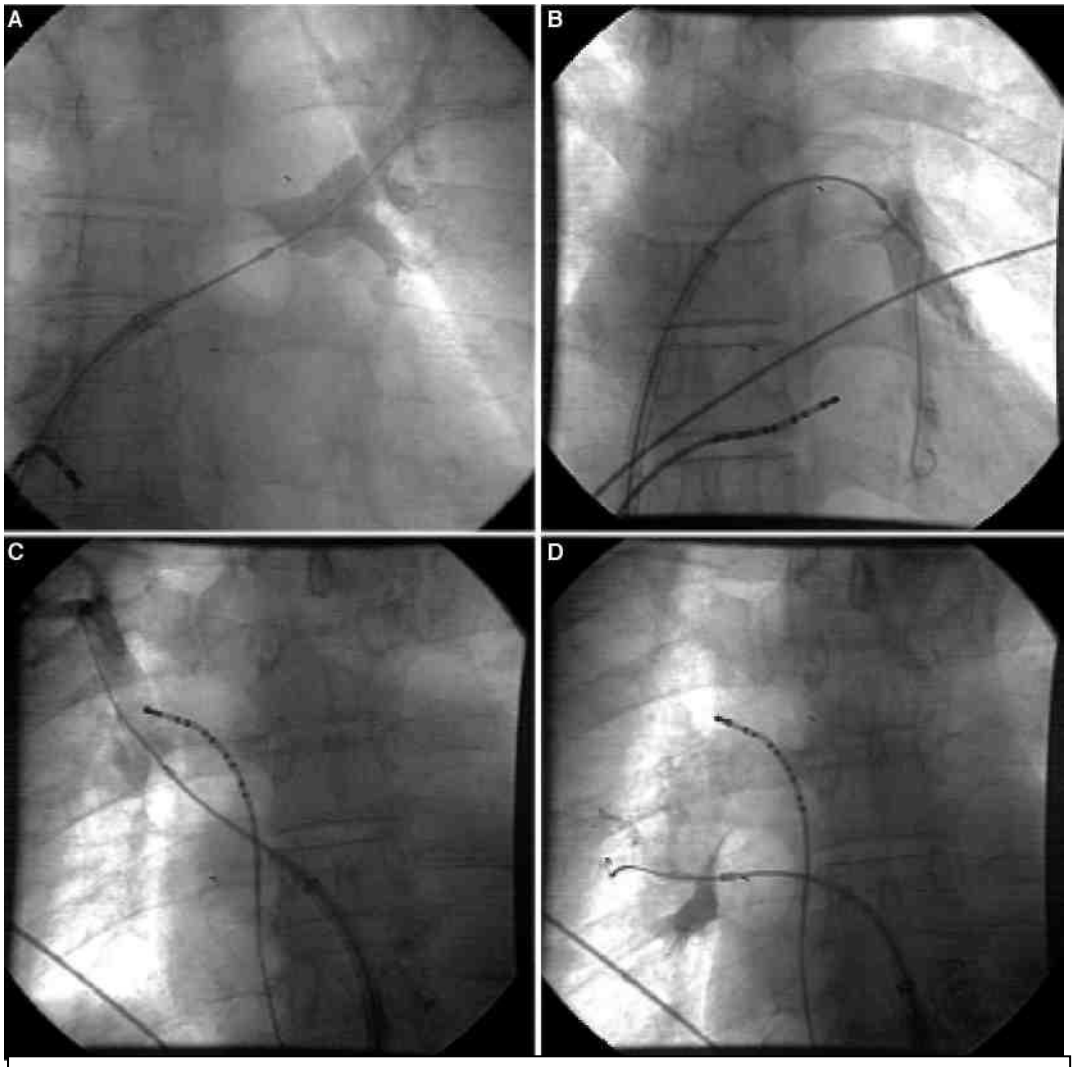


Figure 3. Checking the patency of the pulmonary vein by infusion of diluted contrast agent. Cryoballoon is firstly inflated in the left atrium, then positioned in orifices of the left upper (A), and lower (B), right upper (C), and lower (D) PVs.

If PV isolation could not be achieved, the targeted vein was again subjected to cryoablation. The sheath in the right femoral vein was removed soon after completion of the procedure, while sheaths in the left femoral artery, and vein were withdrawn 4 hours after the last dose of heparin.

Postablation follow-up

Soon after the procedure, and before hospital discharge, all patients underwent transthoracic echocardiographic examinations to evaluate the presence of pericardial effusion. Four or six hours after the operation the first warfarin dose was instituted, and concomitantly,1mg/kg IV enoxaparine was administered at 12-hour intervals. Following the procedure the patients were followed up in an intensive care unit under close hemodynamic, and ECG monitorization. At hospital discharge all patients were prescribed anticoagulation with warfarin to be continued for at least 3 months, and antiarrhytmic therapy according to the attending physician's preferrence. Evaluation performed at the end of the third months, and selection of antiarrhytmic therapy, and anticoagulation therapy based on CHA_2DS_2Vasc score were left to the discretion of the attending physician.

All patients were summoned for control visits to be scheduled 3, 6, and 12 months later. At each control visit complaints of the patients were questioned. All patients underwent 12-lead ECG, standard transthoracic echocardiographic examinations, and 24-hour Holter monitorization independent of their symptoms.

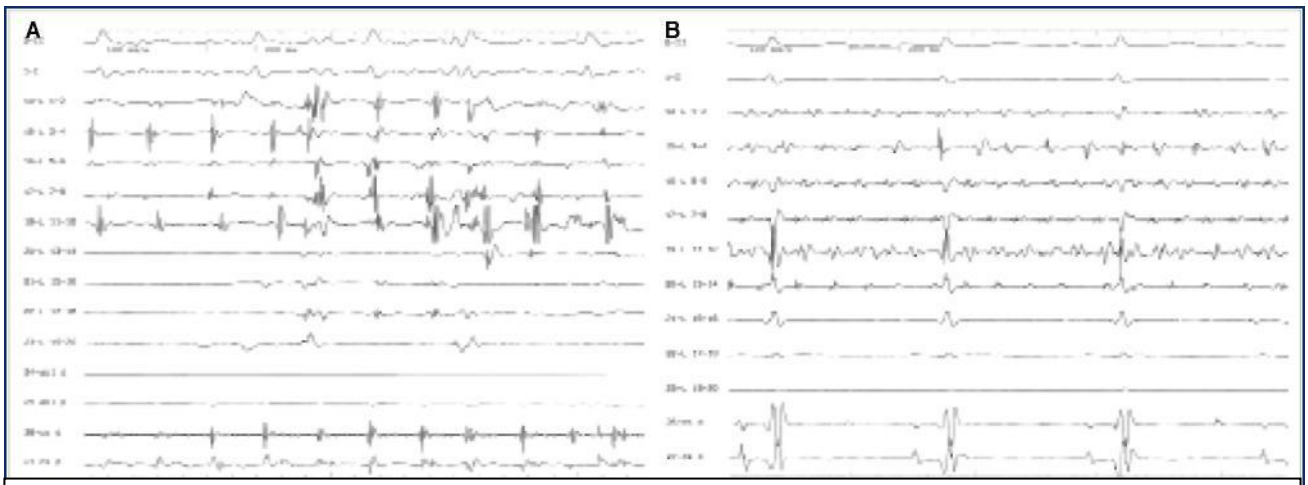
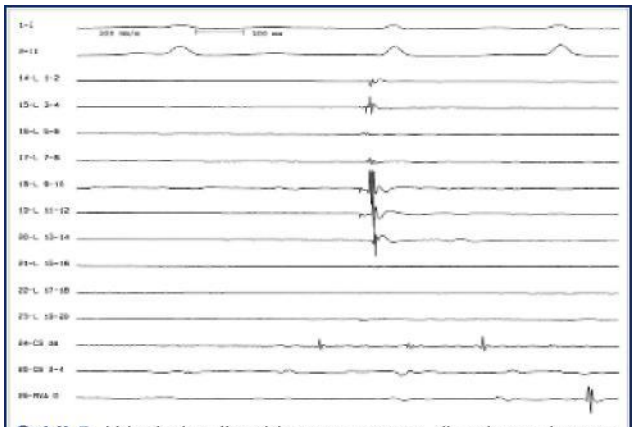


Figure 4. **(A)** Recordings of irregular potentials stemming from the left upper pulmonary vein, and coronary sinus obtained before cryoballoon ablation in a patient with atrial fibrillation.**(B)** after cryoablation, patient's heart rates returned to the sinus rhythm, while irregular potentials persisted as observed in tracings obtained from pulmonary vein

Since mechanical damage, inflammation, and modification of the autonomic nervous system induce marked changes in the myocardial conductivity, and refractoriness, the first 3 months after ablation procedure was defined as 'blanking period.' During this time interval, episodes of AF, atrial flutter or tachycardia lasting longer than 30 secs as detected by ECG or recording devices were considered as "early recurrences." Episodes of AF, atrial flutter or tachycardia developed after the blanking period, and lasted longer than 30 secs were considered as " recurrences."

Variables predicting postablation recurrences

For the evaluation of postablation recurrences, clinical variables as gender, age, history of AF (its type, duration, EHRA score), AF-related cardiovascular diseases (coronary artery disease, hypertension, heart failure), smoking status, alcohol consumption, antiarrhytmic drug use, and echocardiographic variables as diameters of the left atria, and ventricles, left ventricular ejection fraction, severity of mitral regurgitation, pulmonary artery systolic pressure, finally variables related to the ablative procedure as number of PVs, and freeze cycles, maximal cryoablation temperature, and development of recurrences during the blanking period were examined.



Şekil 5. Kriyobalon ile ablasyon sonrası disosiye pulmoner ven potansiyeli izleniyor.

Statistical analysis

For statistical analyses, SPSS 20.0 program was used. Numerical variables with normal distribution were expressed as mean ± standard deviation, and those with non-normal distribution as median, minimal, and maximal values, while categorical variables were indicated as percentages. Concordance of parametres to a normal distribution pattern was checked using Kolmogorov-Smirnov, and Shapiro-Wilk tests, and paired t test was used for those with a normal distribution pattern. For the comparison of non-parametric variables Mann-Whitney U, and Wilcoxon signed Rank test were employed Uni- and multivariate logistic regression analyses were performed to determine the correlation between variables, and recurrences. Procedural success rates were demonstrated on a Kaplan-Meier curve. P <0.05 was accepted as statistically significant.

RESULTS

A total of 236 patients (126 men, 110 women; mean age, 54.6±10.45 yrs; range 16-78 yrs) were enrolled in the study, and monitored. Study group consisted of patients with 188 (79.6 %) paroxysmal, and 48 (20.4 %) persistent AF. Baseline characteristics of the study group are shown in Table 1.

The patients had AF for an average of 8.8±5.8 years (1-22 yrs). A mean number of 1.85 ± 0.5 antiarrhytmic drugs failed to treat AF. Median EHRA score of the complaints elicited during anamnesis was in EHRA III category (range: EHRA II-IV) During preprocedural period, the patients were using warfarin (n=188 patients; 32.8 %), clopidogrel (n=24; 1 %), and aspirin (n=180; 76.2 %).

Features related to cryoballoon ablation procedure are shown in detail (Table 2). A 28-mm balloon was used for all patients. Acute procedural success (≥3 PV isolation) was achieved in 99.5 % (975/980) of the PVs intervened. For each PV, an average of two trials (range, 2-5) of cryoballoon ablation were attempted. Marked decreases in procedural, and fluoroscopy times were achieved near termination of the learning curve of the procedure. Mean procedural, and fluoroscopy times were 72.5±5.3 (50-90), and 14±3.5 (12-24) mins respectively. Vagal reaction developed in 48 (20.3) patients during the application of the procedure.

Severe bradychardia, and asystole developed in 15 (6.3 %) patients, and persisted despite atropin use which required temporary ventricular pacing.

Complications

Major (n= 3; 1.2 %), and minor (n=11; 4.6 %) complications were also observed (Table 2). As major complications, pericardial tamponade requiring percutaneous drainage (n=2), and right femoral arteriovenous fistula necessitating surgical repair (n=1) developed. Minor complications as transient phrenic nerve paralysis which was relieved during the procedure (n=3), inguinal hematoma and/or pseudoaneurysm which did not necessitated any intervention (n=8) were observed.

Follow-up

The patients were followed up for a median period of 14 months (3-24 mos). During the blanking period, early recurrences were observed in a total of 19 (8 %) patients, and AF episodes terminated spontaneously in 14 of them, while electrical cardioversion was required for 5 patients. Antiarrhytmic drugs of the patients were not changed. Following the end of the blanking period recurrences developed in 10 of 19 patients who had experienced early recurrences.

Table 1. Baseline characteristics of the study group

	n	%	Mean ± SD / Median
Age (yrs)			54.6±10.45 (16-78)
Gender (male)	126	54.0	
CAD	23	9.7	
Hypertensives	95	40.2	
Alcohol consumption	18	7.6	
Smoking	76	32.0	
Type of AF			
Paroxysmal	188	79.6	
Persistent	48	20.4	
Duration of AF (yrs)	93	39.4	8.8±5.8 (1-22)
Amiodaron use			
Left atrial AP diameter (mm)			39.04±5.26 (28-54)
Left ventricular EF (%)			64.5±5.8
Number of ineffective antiarrhytmic drugs			1.85±0.
EHRA score			5 3 (2-
Follow-up period (mos)			14 (3-24)

SD: standard deviation SS: CAD: coronary artery disease; AF: Atrial fibrillation; AP: Anteroposterior; EF: Ejection fraction; EHRA: European Heart Rhythm Association.

Table 2. Characteristics of the ablative procedure

Anatomical features	n	%	Mean.±SD / Median
Number of pulmonary veins intervened			4.23±0.5 (3-6)
Common left pulmonary vein (n)	36	15.2	
Common right pulmonary vein (n)	5	2.1	
Procedural particulars			
Acute procedural success rate		99.5	975/980
Procedural time (min)			72.5±5.3 (50-90)
Floroscopy time (min)			14±3.5 (12-24)
Cryoballoon ablation per pulmonary vein			2 (2-5)
Complications			
Tamponade requiring percutaneous drainage	2	0.8	
Femoral AV fistula requiring surgical repair	1	0.4	
Transient phrenic nerve paralysis	3	1.3	
Hematoma, and psedudoaneurym not requiring any intervention İ	8	3.3	
Intraprocedural vagal reaction	48	20.3	
Postprocedural pericardial effusion	25	10.5	

SD, standard deviation.

In 74.5 % of the all study group, and 80.6 % of the patients with AF, and 49.2 % of those with persistent AF, AF episodes were not seen after 3rd months of the follow-up period (Figure 6). Following the blanking period AF recurred in 60 (25.5 %) patients. During follow-up period RF ablation of AF was performed in 10 (16.6 %) patients with recurrences, and in all patients, PV reconnections were seen (at a level above left lower PV in 4, at orifice of the right lower PV in 4, and at orifices of both PVs in 2 patients, respectively). The remaining 50 (83.4 %) patients remained asymptomatic during the follow-up period with antiarrhytmic drug therapy. In a multivariate regression analysis smoking status, body mass index, type of AF, duration of AF, dimensions of the left atrium, and early recurrence were detected as predictors of recurrences after the 3.th month of the follow-up period (Table 3).

DISCUSSION

According to the outcomes of this study, during a median follow-up period of 14 months, 80.6 % of patients with paroxysmal AF, and 49.2 % of those with persistent AF were monitored. During the follow-up period, as predictors of recurrences, smoking status, body mass index, non-paroxysmal AF, duration of AF, dimensions of the left atrium, and early recurrences were found to be statistically significant.

Complication rate was detected to be relatively lower.

Catheter-based PV isolation is a treatment method with established efficacy in cases where pharmacotherapy failed.[4] In AF ablation with RF, predetermined foci around PVs were ablated circumferentially using focal energy.[4] This complex approach has many limitations, and requires electroanatomical mapping. Intact areas between ablated foci may induce reconnections, and recurrent AFs.[15,16] Therefore new ablation technologies have been developed. Cryoballoon technique is one of these innovatiıons. In the cryoballoon technique, cryoballoon is inflated within the orifice of PV, and cooled down to –80ºC using N_2O (nitrous oxide). Cryoballoon technique has many advantages. Firstly it does not require prior mapping with shorter fluoroscopy times Besides, all aberrant foci around PV can be circumferentially ablated using cryoenergy with steady contact with the target tissue. Although the balloon in the PV orifice is positioned more distally when compared with the catheter-based method, it ensures circumferential and more durable, and complete PV isolation without leaving intact spaces between ablated foci. [17-19] Two small-scale studies which compare RF, and cryoballoon ablation found comparable success rates..[20,21]

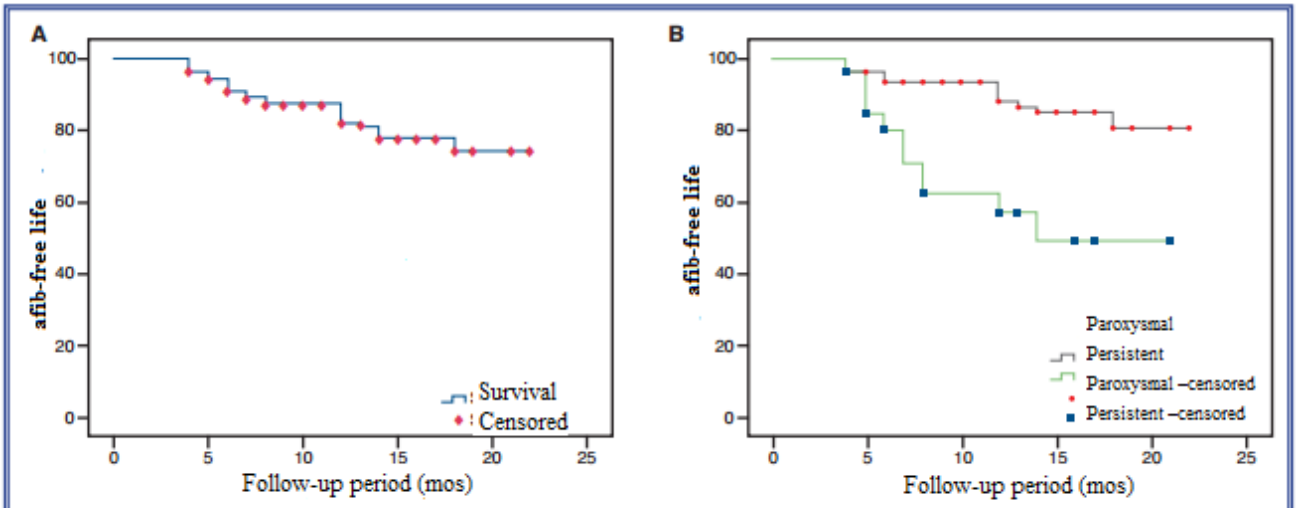


Figure 6 (A) Duration of afib-free life during follow-up periods of all the group, and paroxysmal or persistent AF patients as plotted on a Kaplan-Meier curve

Up to date nearly 20.000 patients worlwide have undergone PV ablation with cryoballoon technique. In the first randomized trial performed by cryoballoon technique, [Sustained Treatment of Paroxysmal Atrial Fibrillation (STOP-AF)] the patients were randomized into antiarrhytmic drug, and cryoablation arms. During 12 months of the follow-up period, 69.9 % of the patients in the cryoballoon group, while only 7.3 % of those in the antiarrhytmic drug group did not experience any AF episodes.[22] Recently, Andrade et al .[23] published the outcomes of early phase experiences with cryoballoon ablation. Based on the results of this meta-analysis, complete PV isolation was ensured in more than 98 % of the patients. When the first postoperative 3 months (blanking period) was taken into consideration the authors reported that after a single cryoballoon procedure 73, and 45.1 % of paroxysmal AF, and persistent AF patients had not experienced recurrences, respectively.[23] However, Calkins et al reported the incidence of afib-free life as 50-64% during 14 months of the follow-up period. In their prospective cohort studies, Weerasooriya et al.[24] reported mean incidence of afib-free life for one year as %39.8±5.1.

According to our results which are in accordance with the literature findings, during a median follow-up period of 14 months, the rate of afib-free life was 80.6 % for paroxysmal, and 49.2 % for persistent AF, respectively. The most frequent cause of recurrences after catheter-based paroxysmal AF ablation is PV reconnection which is seen in lower segments, and left atrial appendage-PV junction after use of 28-mm cryoballoon [20,25] In our center, patients who develop recurrences after cryoballoon application, radiofrequency AF ablastion is performed. We also applied RF ablation in 10 (16.6 %) patients with recurrent AF, and observed PV reconnections in all of them.

PV reconnection is the most frequent reason for the development of recurrences after catheter-based AF ablation.[25] Inability to achive sustainability of the focal lesions created by RF ablation, and anatomical difficulties encountered during cryoballoon ablation are culprit etiological factors leading to PV reconnections [18]

Table 3. Predictors of recurrences after cryoablation as estimated in multivariate regression analysis

	b	95% CI	p
Non-paroxysmal atrial fibrillation	1.147	1.057-9.375	0.040
Duration of atrial fibrillation (yrs)	0.104	1.005-1.224	0.039
Diameter of the left atrium (mm)	0.147	1.047-1.281	**0.004**
Smoking status	1.184	1.175-9.084	0.023
Body mass index (kg/m^2)	1.276	1.077-1.513	**0.005**
Early recurrence	1.324	1.152-12.124	**0.0001**

Many studies have shown the efficacy of RF on the choice of re-ablation technique following a recurrent episode of AF, however adequate data are not available on reapplication of the cryoballoon technique. In the literature, many authors have reported electrically intact non-ablated in- between spaces after first application of AF ablation, and asserted that reablation in patients with recurrences ensured a 50 % afib-free life for 12 months [26,27] Schade et al [28] achieved 60 % (23/47 patients) success rates during 12 years of the follow-up period in patients who had undergone reablation with cryoballoon technique after recurrent AF episodes.

Pokushalov et al [29] compared RF (n=40) and/or cryoballoon (n=40) as reablation techniques in 80 patients with recurrences after AF ablation with RF, and detected rates of afib-free life within 12 months of the follow-up period as 59, and 38 % in groups who had undergone only RF or cryoballoon ablation modalities, respectively (p=0.021). Because of the recurrences after AF ablation with cryoballoon technique are related mostly to anatomic factors, targeting only reconnection points during AF ablation, and lack of adequate data supporting the preference of cryoballoon technique for reablation, RF ablation appears to be more appropriate as a reablation technique.[25,30]

Many studies have been performed on clinical predictors of efficacy of AF ablation.[31-36] At least one study reported non-paroxysmal AF (especially prolonged persiştent AF) , sleep apnea, obesity, increased left atrial diameter, advanced age, hypertension, and atrial fibrosis as detected by MRI among predictors of unfavourable outcomes. In 11 of 17 studies, type of AF was not found to be significant in the prediction of recurrences, in 6 studies non-paroxysmal AF was detected as independent predictor of recurrent AF (hazard ratio: 1.8-22). In 4 out of 20 studies investigating the impact of left atrial dimensions on recurrences of AF, increased left atrial diameter was found to be a predictor of recurrences. In our study, non-paroxysmal AF, increased AF episodes, increments in left atrial diameter, body mass index, smoking, and early recurrences were revealed as independent predictors of recurrences. Distinct from previous studies, as a determinant of recurrences smoking contributes to the inflammatory process, and prolonged AF episodes was found to be a predictor of recurrences because of its role in triggering structural remodelling in the long-term.

Major complications were reported in 5-6 % of the patients who had undergone radiofrequency ablation of AF.[8,10,11] However acute procedural complication rates in AF ablation with cryoballoon technique are relatively lower (<3-5 %) [8,10,11,37] In a meta-analysis, ischemic attack or stroke (0.3 %), cardiac tamponade (0.6 %), and inguinal region complications (1.8 %) were stated as complications of cryoballoon ablation technique .[23] In the same meta-analysis, following cryoballoon procedure, development of pulmonary stenosis, was rarely (0.17 %) reported, while atrioesophageal fistula was not found. When compared with RF ablation, global complication rate was less frequently reported for cryoballoon AF ablation technique. Still, three major complications (phrenic nerve paralysis, PV stenosis, and systemic thromboembolism) retain their significance. In animal studies, Sarabanda et al [38] observed phrenic nerve paralysis as the most frequent complication, and in clinical studies it was reported in an average of 6 % (3-11 %) of the cases. [23,39] Though the most frequently seen complication is phrenic nerve paralysis, Phrenic nerve paralysis is transient, and in only < 0.4 % of the patients, it persists longer than a year.[23] Also in our study, transient phrenic nerve paralysis developed in 3 patients (1.2 %). The most significant factors contributing to the relatively lower rates of complications in our study, are doubtlessly related to manual abdominal examination during right-sided PV isolation, and termination of the cryoablation procedure when decrease in the strength of bowel contractions is perceived. The frequency of symptomatic or intervention requiring PV stenosis for cryoballoon, and RF ablation techniques has been reported as 0.17, and 0.1-0.3 %, respectively[8,10,11] In our study symptomatic or intervention requiring PV stenosis was not observed. Systemic thromboembolism was reported in 0.32 % of the cases which is relatively lower than those observed in conventional RF ablation (0.3-0.94%) [8,10,11] Hemorrhagic or ischemic stroke was not seen in our series. Generally, our complication rate was found to be relatively lower.

Because of presence of unablated intact in-between spaces generated by linear lesions after radiofrequency ablation, development of left atrial tachycardia has been prevalently reported.[40] However incidence of atrial tachycardia after cryoballoon ablation has been indicated at a rate of 0.8-1.7 percent.[12,13] In our study, postprocedural atrial tachycardia was not detected. This outcome was largely thought to stem from generation of circular lesions relatively closer to PV by cryoballoon technique. In our study, mean procedural, and fluoroscopy times were 72.5±5.3 (50-90) and 14±3.5 (12-24) minutes, respectively which are shorter when compared with those of other studies performed using RF, and cryoballoon ablation techniques. In the first 30 patients enrolled in our study, procedural, and fluoroscopy times were longer, while they markedly decreased in line with the progress in the learning curve. Relatively shorter procedural, and fluoroscopy times might be attributed to a single transseptal puncture used in our study, evaluation of PV anatomy by MSCT before the procedure, and ample experience of our center with AF ablation technique

This is the first study which reflects experience with cryoballoon AF ablation in Turkey. Success rates of a single procedure at desired levels especially in patients with paroxysmal AF, and relatively lower complication rates demonstrate efficacy, reliability, and safety of cryoballoon ablation in the management of AF. Particularly patients with early recurrences should be closely monitored for recurrences after the blanking period.

Limitations of the study

Relatively shorter follow-up periods with brief montorization phases, inability to recognize silent AF episodes, lack of comparisons with RF ablation technique as for its efficacy, reliability, safety, and cost-effectiveness because of the non-randomized design of the study, and failure to evaluate asymptomatic PV stenosis, and silent episodes of stroke constitute limitations of the study.

Conflict *interest: None declared*

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Key words: Atrial fibrillation/physiopathology/surgery/therapy; electrophysiologic techniques, cardiac; catheter ablation/method; cryosurgery/method; myocardium/pathology; pulmonary veins/surgery.