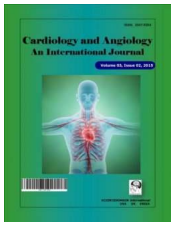

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Catheter Ablation of Atrial Fibrillation: Three-dimensional Transesophageal Echocardiography Provides an Excellent Overview over the Pulmonary Vein Anatomy Facilitating Radiofrequency and Cryoablation Procedures

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Authors' contributions

All authors have made substantial contributions to the design of the study, to the data evaluation and to the drafting of the manuscript. They have approved the current version of the manuscript.

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ABSTRACT

Background: Catheter of atrial fibrillation is still challenging because of the high degree of variability of the pulmonary vein anatomy. Therefore, 3D imaging systems are frequently used prior to an ablation procedure. Three-dimensional transesophageal echocardiography provides an excellent overview over the individual left atrial morphology without some of the limitations associated with other imaging techniques.
Methods: In 50 patients, three-dimensional transesophageal echocardiography was performed immediately prior to an ablation procedure. The images were available throughout the ablation procedure. In most of the patients with paroxysmal atrial fibrillation, the cryoablation technique was used (Arctic Front Balloon, CryoCath Technologies/Medtronic; group A2). In the other patients, a

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circumferential pulmonary vein ablation was performed using the CARTO system (Biosense Webster; group A1 (paroxysmal atrial fibrillation), group B (persistent atrial fibrillation)).
Results: A three-dimensional transesophageal echocardiography could be performed successfully in all patients and all four pulmonary vein ostia could be evaluated in 84% of patients. The image quality was excellent in the majority of patients and several variations of the pulmonary vein anatomy could be visualized precisely. The findings obtained by three-dimensional transesophageal echocardiography correlated well with the pulmonary vein angiographies performed during the ablation procedures. At 24-month follow-up, 76% of all patients were free from an arrhythmia recurrence (group A1: 81.8%, group A2: 78.9%, group B: 70.0%). There were no major complications.
Conclusions: AF ablation procedures can be performed safely and effectively based on prior 3D TEE imaging.

Keywords: Catheter ablation; atrial fibrillation; pulmonary veins; transesophageal echocardiography.

1. INTRODUCTION

Catheter ablation has become the first line of therapy in patients with symptomatic, recurrent, drug-refractory atrial fibrillation (AF; [1-16]). However, it is still challenging because of the high degree of variability of the pulmonary vein (PV) anatomy. Therefore, 3D imaging systems (multi-detector spiral computed tomography (MDCT) or magnetic resonance imaging (MRI)) are frequently used prior to an ablation procedure.

These three-dimensional imaging systems provide detailed information about the left atrial and pulmonary vein morphology. Obviously, the precise knowledge of the left atrial anatomy facilitates the ablation procedures and enhances the safety of these interventions. However, these imaging techniques (MDCT/MRI) are associated with significant limitations (such as radiation exposure (MDCT), inappropriate image quality in the presence of atrial fibrillation with rapid ventricular response (especially MRI) and addtitional costs).

Alternatively, three-dimensional transesophageal echocardiography (3D TEE) provides an excellent overview over the individual left atrial morphology without most of the limitations associated with other imaging techniques [17-25].

Therefore, the aim of our study was to assess the usefulness of 3D transesophageal echocardiography for evaluating the pulmonary vein anatomy prior to catheter ablation of atrial fibrillation. This study summarizes our experience with two different strategies of AF ablation after prior pulmonary vein imaging using three-dimensional transesophageal echocardiography.

2. METHODS

2.1 Patient Population

Fifty patients were enrolled in this study. All of them underwent 3D transesophageal echocardiography immediately before the ablation procedure, so that a 3D TEE reconstruction of the left atrium and the pulmonary veins could be generated. The study cohort comprised all patients who underwent catheter ablation of AF at our institution after prior 3D TEE imaging within the period of time mentioned below (consecutive patients). Patients undergoing catheter ablation without prior 3D TEE imaging were not taken into consideration for this study.

All patients were highly symptomatic and at least one failed attempt of an antiarrhythmic drug therapy was a prerequisite for being accepted for catheter ablation.

Table 1 summarizes clinical characteristics of the patients enrolled in our study. For all patients, this was the first AF ablation procedure.

The ablation procedures were performed at our University Hospital Center between October 2007 and May 2011.

Inclusion criteria were (1) documented episodes of recurrent atrial fibrillation (≥ 30 seconds), (2) severe symptoms despite antiarrhythmic drug therapy (including beta-blockers) or prior attemps of electrical cardioversion, (3) ability and willingness to give informed consent, and (4) age between 18 and 85 years. Patients were not accepted for catheter ablation if one of the following conditions was present: severe valvular heart disease or any other concomitant cardiac

Table 1. Clinical data

	Group A	Group A1	Group A2	Group B	P
Patients	30	11	19	20	0.07
Men : Women	18 : 12	5 : 6	13 : 6	17 : 3	
Age	60.0 years	61.6 years	59.1 years	62.1 years	0.57
Mean (SD)	(9.7 years)	(8.0 years)	(10.7 years)	(8.4 years)	
Cardiac disease					0.05
None	13	8	5	2	
CAD	3	1	2	9	
DCM	0	0	0	1	
Valvular heart disease *	5	1	4	5	
Arterial hypertension	9	1	8	2	
Other	0	0	0	1	
Previous cardiac surgery	1	0	1	0	0.43
Left ventricular ejection fraction	58.0 %	59.1 %	57.4 %	52.6 %	0.06
Mean (SD)	(5.8 %)	(7.4 %)	(4.8 %)	(9.9 %)	
Antiarrhythmic drug therapy prior to the ablation procedure					0.68
- Class Ic (e.g. Flecainide, Propafenone)	1	0	1	2	
- Class III (e.g. Amiodarone, Sotalol)	5	0	5	2	
- Beta-Blocker in combination with a class Ic or class III antiarrhythmic drug	16 / 7	7 / 3	9 / 4	3 / 7	
- Beta-Blocker	1	1	0	6	
- Digitalis	0	0	0	0	
- Other	0	0	0	0	

*CAD = Coronary artery disease; DCM = Dilated cardiomyopathy (left ventricular ejection fraction < 40 %); * not requiring surgery*

disease requiring surgery, severely impaired left ventricular function (left ventricular ejection fraction < 20%), left atrial diameter > 65 mm (parasternal long-axis view), left atrial thrombus, hyperthyroidism, severe renal insufficiency (creatinine ≥ 3 mg/dl) or another severe concomitant illness.

2.2 Cardiac Imaging

In all patients, a three-dimensional transeso-phageal echocardiography was performed immediately before the ablation procedure (X7-2t, 7 MHz; IE 33; Philips Healthcare, Best, The Netherlands). Real-time 3D images of the left atrium were obtained. The images were available throughout the ablation procedures. They were displayed in a synchronised way with the geometry created with the 3D mapping system (if available).

The echocardiographic examination was performed extensively to acquire all relevant information about the left / right atrium, all cardiac valves, the left / right ventricular function and the aorta. In addition, 3D reconstructions of the left atrium and the pulmonary vein ostia were generated. We aimed at visualizing all pulmonary vein ostia precisely in multiplanar views (including 3D color Doppler datasets) and to reveal all variations of the pulmonary vein anatomy (common ostia, accessory pulmonary veins) or the left atrium (very prominent left atrial appendage, extremely short distance between the left atrial appendage and the left superior pulmonary vein). The image quality was classified as (1) good, (2) acceptable or (3) not appropriate (for each pulmonay vein ostium). The grading “good” was used when PV ostia could be visualized precisely. The term “acceptable” was applied if the image quality was impaired (but still sufficient for analysing the PV anatomy). It was

documented which PVs could not be visualized. The variations of the PV anatomy were classified as given in Table 2. The TEE findings were compared with the results of the selective biplane pulmonary vein angiographies performed during the ablation procedure (see Tables 2 and 3). The data was analysed by three experienced cardiologists, who were familiar with three-dimensional transesophageal echocardiography and pulmonary vein imaging (laboratory accredited by the European Association of Echocardiography).

No other imaging techniques (MDCT or MRI) were used before or after the ablation procedures routinely.

2.3 Ablation Procedure

The ablation strategy was depending on the type of atrial fibrillation.

In patients with paroxysmal atrial fibrillation, two strategies were used. In some patients with paroxysmal atrial fibrillation, a cicumferential pulmonary vein ablation was performed in combination with a potential-guided segmental approach in order to achieve complete pulmonary vein isolation (group A1; CARTO system (Biosense Webster, Diamond Bar, CA, USA)). In most of the patients with paroxysmal AF, the cryoballoon technique (Medtronic, Minneapolis, MN, USA) was used (group A2). In patients with persistent atrial fibrillation, a circumferential pulmonary vein ablation was performed in combination with a potential-guided segmental approach to achieve complete pulmonary vein isolation ([20]; group B). Furthermore, a linear lesion was created at the roof of the left atrium in some patients. In addition, catheter ablation of the mitral isthmus was performed in selected cases (CARTO system ((Biosense Webster)).

AF ablation procedures were performed under conscious sedation at our institution. For the electrophysiological study, vascular access was obtained via both femoral veins and the left femoral artery. A 2500-U IV bolus of heparin was given shortly thereafter. First, a 6-F decapolar catheter (Bard, Electrophysiology Division, Lowell, MA, USA) was positioned within the coronary sinus (CS). Then, a single (or double) transseptal puncture was performed under fluoroscopic guidance. Immediately before the transseptal puncture, a 5-F catheter was placed in the ascending aorta to mark this area and to enhance the safety of the procedure. In some patients no transseptal puncture was necessary because of a patent foramen ovale or a defect of the atrial septum.

In group A1 and in group B, an irrigated-tip CARTO ablation catheter (NAVI-STAR; 7F, D-type; 3.5-mm-tip; Biosense Webster) was positioned within the left atrium thereafter. Furthermore, a Lasso-catheter 2515; 7F; Biosense Webster) was placed in the left atrium.

Then, a second iv bolus of heparin was administered. During the procedure, the activated clotting time (ACT) was determined at regular intervals to ensure an adequate anticoagulation (ACT between 250 and 300 s). Then, a selective biplane pulmonary vein angiography was performed (LAO (45°) projection and RAO (30°) view). After that, a geometry of the left atrium was created using the CARTO system and compared to the 3D TEE reconstructions. This allowed to correct potential shortcomings of the geometry created with the mapping system. The 3D TEE reconstructions were displayed in a synchronized way throughout the ablation procedure.

In the majority of patients, a standard stomach tube (Flocare Nutrisoft M, Nurtica Healthcare, Châtel-St.Denis, Switzerland) had been introduced via a nasogastric route immediately before the ablation procedure in order to mark the esophagus. Radiofrequency (RF) energy applications were avoided if there was a close anatomical relationship to the esophagus (or the power output was reduced as described previously [19]).

First, a circumferential pulmonary vein ablation was performed in all patients in group A1 and in group B targeting the both left-sided pulmonary veins (43°C; 30 W (posterior wall) - 40 W (anterior wall)). In addition, a Lasso catheter was placed in the left superior or left inferior pulmonary vein. After completing the circumferential ablation line around the left-sided pulmonary veins, the left superior pulmonary vein and the left inferior pulmonary vein were reevaluated using the circular mapping catheter. If there was no complete PV isolation additional RF energy applications (43°C; (25-) 30 W) were applied using a segmental approach (during sinus rhythm / CS pacing or ongoing AF). If the isolation of the

Table 2. Left atrial anatomy (assessed by 3D TEE* and/or by invasive PV angiography)**

	3D TEE	Invasive pulmonary vein angiography
Common PV ostium	2	2
(Left PVs / right PVs)	(1 / 1)	(1 / 1)
Accessory PVs	1	1
(Left PVs / right PVs)	(0 / 1)	(0 / 1)
Early PV branching	0	3
LSPV		0
LIPV		0
RSPV		2
RIPV		1
Extremely short distance between the LAA and the LSPV	3	n.d.
Very prominent left atrial appendage	2	n.d.

LAA = Left atrial appendage; LIPV = Left inferior pulmonary vein; LSPV = Left superior pulmonary vein; PV(s) = Pulmonary vein(s); RIPV = Right inferior pulmonary vein; RSPV: Right superior pulmonary vein; 3D TEE = Three-dimensional transesophageal echocardiography, n.d. = Not determined

Table 3. Mean diameter of the left-sided and right-sided pulmonary veins (as assessed by three-dimensional transesophageal echocardiography and by invasive pulmonary vein angiography)

	LSPV	LIPV	RSPV	RIPV
Diameter of the main trunk* Mean (SD)	13.9 mm (3.9 mm)	13.4 mm (3.9 mm)	14.0 mm (2.8 mm)	13.1 mm (3.2 mm)
Diameter of the main trunk** Mean (SD)	17.3 mm (3.1 mm)	16.8 mm (2.9 mm)	16.1 mm (2.4 mm)	14.9 mm (2.2 mm)
P	0.41	0.27	0.17	0.43

** as assessed by three-dimensional transesophageal echocardiography*
*** as assessed by invasive pulmonary vein angiography (biplane)*
LIPV = Left inferior pulmonary vein; LSPV = Left superior pulmonary vein; RIPV = Right inferior pulmonary vein; RSPV: Right superior pulmonary vein

left-sided PVs was assumed to be complete, the right-sided PVs were targeted in the same way.

If atrial fibrillation was still present after completing the circumferential ablation lines and no residual PV potentials could be identified, an electrical cardioversion was performed. Then, all four pulmonary veins were reevaluated using the circumferential mapping catheter.

Futhermore, a linear lesion at the LA roof was created in some patients in group B (43℃; 30-35 W). In a few patients in group B, an additional mitral isthmus ablation was performed (especially if there was evidence for left atrial isthmus-dependent flutter (43℃; 35-40 W)). Finally, the linear lesions at the LA roof were reevaluated during sinus rhythm. The ablation catheter was navigated back along the entire lesion to assess the presence of low-amplitude electrograms and the presence of double potentials or fractionated electrograms. If sharp high-amplitude electrograms were noted, additional RF applications were delivered at these sites in order to achieve a complete ablation line. In addition, the linear lesions to the mitral annulus were reevaluated (anterior mitral isthmus line).

At the end of the ablation procedure, the completeness of the pulmonary vein isolation and of all linear lesions was reassessed after a waiting period of at least 20 minutes. Repeat selective pulmonary vein angiographies were performed of all PVs. In addition, catheter ablation of the right atrial isthmus was performed in patients with inducible or clinically documented

episodes of typical atrial flutter. The completeness of the right atrial isthmus lines was confirmed by differential pacing maneuvers in all cases.

For the ablation procedure, a Bard EP system (LabSystem Pro, EP Recording System; Bard, Electrophysiology Division, Lowell, MA, USA) and a Stockert RF generator (EP-shuttle; Stockert, Freiburg, Germany) were used. High-resolution X-ray imaging was provided by a Philips device (Philips Medical Systems, Best, The Netherlands).

Some modifications were made in group A2. In these patients, the cryoballoon technique was used. After performing the pulmonary vein angiographies, the decision was made to use a 23 mm or 28 mm cryoballoon (Arctic Front; Medtronic, Minneapolis, MN, USA). The choice of the balloon diameter was determined by the left atrial anatomy observed on the pre-procedural 3D TEE examinations as well as by the intraprocedural PV angiographies. Once the FlexCath Sheath (Medtronic) had been introduced into the left atrium via a transseptal puncture, the Arctic Front cryocatheter was passed through the FlexCath lumen over the guide wire and guided into the left atrium in a deflated state. Then, the guide wire was placed in the left superior pulmonary vein (LSPV). After that, the cryoballoon was inflated in the atrium and positioned at the ostium of the LSPV. Balloon position was verified by injection of contrast. Every effort was made to obtain a complete occlusion with contrast remaining in the vein. Then, a minimum of two cryoapplications was performed (lasting 5 minutes each). After that, successful pulmonary vein isolation was verified using a circular mapping catheter (Lasso 2515; Biosense Webster). In some patients, we used the Achieve inner lumen circular mapping catheter (loop diameter: 15 or 20 mm; Medtronic) instead of a Lasso catheter and a standard guide wire. If there was no complete PV isolation additional cryoapplications were performed (maximum duration: 5 minutes/cryoapplication). After having completed the isolation of the LSPV, the LIPV was targeted in the same way. Then, cryoablation of the right superior and right inferior pulmonary vein was performed. During cryoablation of the antrum of the right-sided pulmonary veins, diaphragm movement was monitored by either continuous phrenic nerve stimulation with a right atrial stimulation catheter positioned superiorly compared with the balloon position or by continuous monitoring of the phrenic movement during spontaneous breathing [26]. Finally, the completeness of the isolation of all four pulmonary veins was reassessed after a waiting period of at least 20 minutes. Additional cryoapplications were delivered if necessary. In no complete PV isolation could be achieved with a maximum of 5 cryoapplications using the cryoballoon device chosen at the beginning of the procedure a cryoballoon with a different diameter or a standard cryoablation catheter (Frezzor Max; Medtronic; targeted temperature: - 75℃; maximum duration of a single cryoapplication: 4 minutes) was used for further cryoapplications.

During the cryoablation procedure activated clotting time was maintained between 250 and 350 seconds. In some patients in group A2, three-dimensional transesophageal echocardiography was used to guide the transseptal puncture and the positioning of the cryoballoon.

2.4 Follow-up

After hospital discharge, patients were seen regularly on an outpatient basis. One month after the procedure, a physical examination, a resting electrocardiogram (ECG) and a transthoracic echocardiogram were performed. The patients were questioned whether there was any evidence for an arrhythmia recurrence. In addition, a long-term ECG recording (24-h) was performed.

Three months after the ablation procedure, the patients were re-examined in the same way except for the fact that a 7-day Holter monitoring was performed and that each patient underwent a repeat three-dimensional transesophageal echocardiography to rule out a pulmonary vein stenosis. Then, the patients were seen at 3-month intervals if asymptomatic. If there was an arrhythmia recurrence or other problems occurred, the further follow-up and future strategy (e.g. medical therapy, electrical cardioversion, repeat ablation procedure) were planned on an individual basis.

Twelve months and twenty-four months after the ablation procedure another 7-day Holter monitoring was performed. A blanking period of 3 months was employed after ablation when evaluating the follow-up results.

In addition, all patients were given a questionnaire 24 months after the ablation procedure. The aim of this questionnaire was to evaluate the clinical status of the patients and to reveal whether there was any evidence for

arrhythmia recurrences not detected by the long-term ECG recordings [20].

Oral anticoagulation was continued for at least 3 months after the procedure in all patients and was discontinued only in patients with a CHADS2 score ≤ 1 thereafter. Since October 2010 the CHADS2-VASc score was used for risk assessment and oral anticoagulation was only discontinued in patients with a CHADS2-VASc score ≤ 1 three months after the ablation procedure (vitamin K antagonist / novel oral anticoagulants). During the first three months after catheter ablation the patients received the same antiarrhythmic medication as prior to the ablation procedure. If there was no evidence for an arrhythmia recurrence all antiarrhythmic drugs were discontinued thereafter except for beta-blockers.

2.5 Statistical Analysis

Clinical characteristics of the three study groups were compared at baseline to discover potential sources of bias. All parameters with a normal distribution are given as mean (± 1 standard deviation (SD)). Age, left ventricular ejection fraction, total procedure time, fluoroscopy dosage and follow-up duration were compared using an one-way ANOVA. All other parameters (underlying cardiac disease, gender) were analysed using the chi-square test.

The chi-square test was also used for analysing the clinical endpoints (arrhythmia recurrence rate at 12/24-month follow-up). The diameters of all pulmonary veins assessed by 3D TEE and invasive angiography were compared using t-tests.

Significance was accepted if the P value was ≤ 0.05.

The statistical package of JMP (Version 3.2.6, SAS Institute, Cary, NC, USA) was used for data analysis.

3. RESULTS

Fifty patients were enrolled in this study between October 2007 and May 2011. All of them suffered from recurrent paroxysmal or persistent atrial fibrillation. In all patients, catheter ablation was performed after prior 3D TEE data acquisition. Catheter ablation was performed for paroxysmal atrial fibrillation in 30 patients and for persistent atrial fibrillation in 20 patients. In all patients, this was the first ablation procedure. The ablation procedure could be performed as planned in all patients.

3.1 Ablation Strategy

In some patients with paroxysmal atrial fibrillation an anatomically-based circumferential pulmonary vein ablation in combination with a potential-guided segmental approach was performed (group A1: 11 patients; Carto system (Biosense Webster)).

In the remaining 19 patients with paroxysmal atrial fibrillation, the cryoballoon technique was used (group A2; Medtronic). In all of them, a 28 mm cryoballoon was chosen at the beginning of the procedure. In 4 patients, a second cryoballoon (23 mm; n = 1) or a standard cryoablation catheter (Freezor Max, Medtronic; n = 3) had to be used to achieve complete pulmonary vein isolation.

In all patients with persistent atrial fibrillation (n = 20), an anatomically-based circumferential pulmonary vein ablation in combination with a potential-guided segmental strategy was performed as the standard approach (group B). Furthermore, a linear lesion was created at the roof of the left atrium in 7 patients with persistent AF. In 2 patients in group B, additional catheter ablation of the mitral isthmus was performed.

In addition, catheter ablation of the right atrial isthmus was performed in 5 patients in group A (A1: 4 patients, A2: 1 patient) and in 2 patients in group B.

3.2 Procedural Results

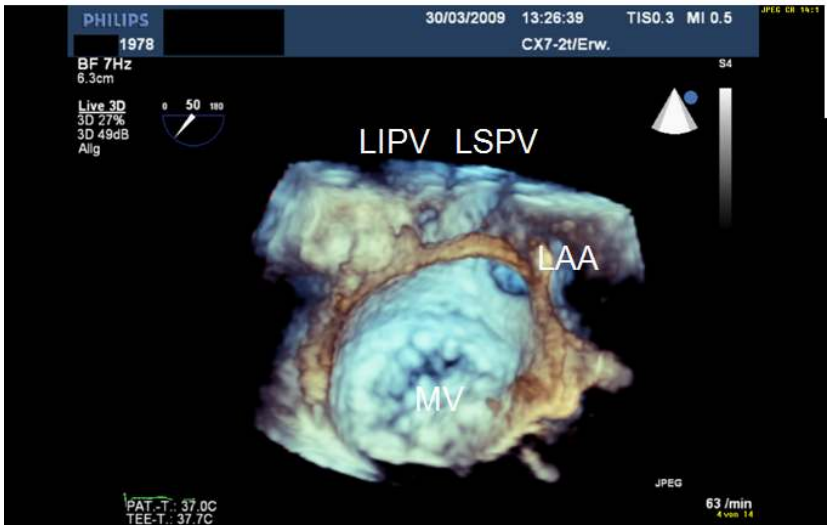
The ablation procedure could be performed as planned in all patients. The mean procedure time was 171 minutes (SD ± 49 minutes) in group A (A1: 199 minutes (SD ± 36 minutes) / A2: 158 minutes (SD ± 48 minutes)) and 163 minutes (SD ± 51 minutes) in group B (P = 0.1). This included all preparations and a waiting period (20 minutes) at the end of the procedure for a final reevaluation of the completeness of the pulmonary vein isolation/linear lesions. The mean fluoroscopy dosage was 2918 cGycm² (SD ± 1676 cGycm²) in group A (A1: 2639 cGycm² (SD ± 1516 cGycm²) / A2: 3079 cGycm² (SD ± 1769 cGycm²)) and 3013 cGycm² (SD ± 1169 cGycm²) in group B (P = 0.3).

In group A1, an anatomically-based circumferential pulmonary vein ablation in

combination with a potential-guided segmental approach was performed successfully in all patients. In this group, all four pulmonary veins could be isolated successfully in all patients (documented using a circular mapping catheter). The circumferential strategy had to be combined with potential-guided segmental RF-applications in the majority of patients (7/11).

In group A2, all cryoablation procedures could be completed successfully using this technique. A mean number of 3.9 PVs (SD ± 0.7 PVs) were isolated per patient.

In group B, the circumferential ablation lines around the left-sided and right-sided pulmonary veins could be performed successfully in all patients according to anatomical criteria. However, this did not result in complete pulmonary vein isolation in most cases (when using the aforementioned moderate ablation parameter settings as well as a sufficient safety margin to the pulmonary vein ostia and the esophagus). Therefore, this circumferential strategy had to be combined with a potential-guided segmental approach to achieve complete pulmonary vein isolation in the majority of patients in group B (12 of 20 patients). Finally, a mean number of 3.8 pulmonary veins (SD ± 0.9 PVs) were isolated per patient in group B.



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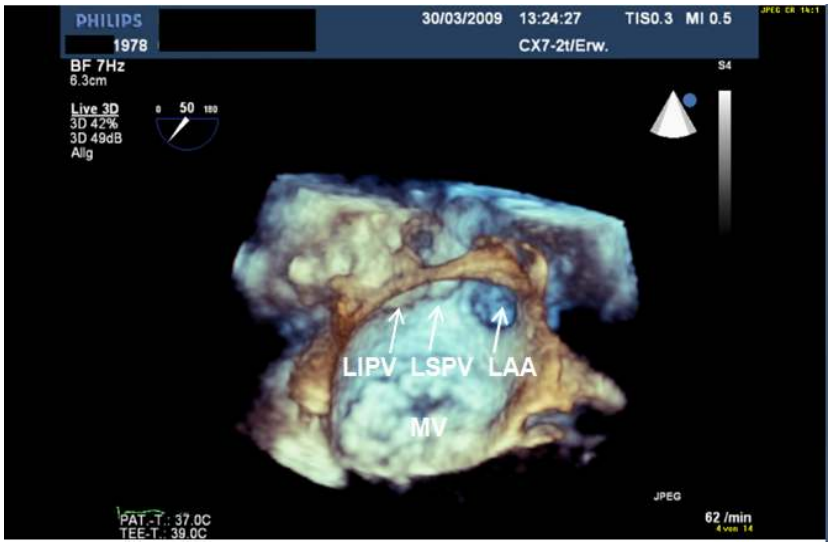

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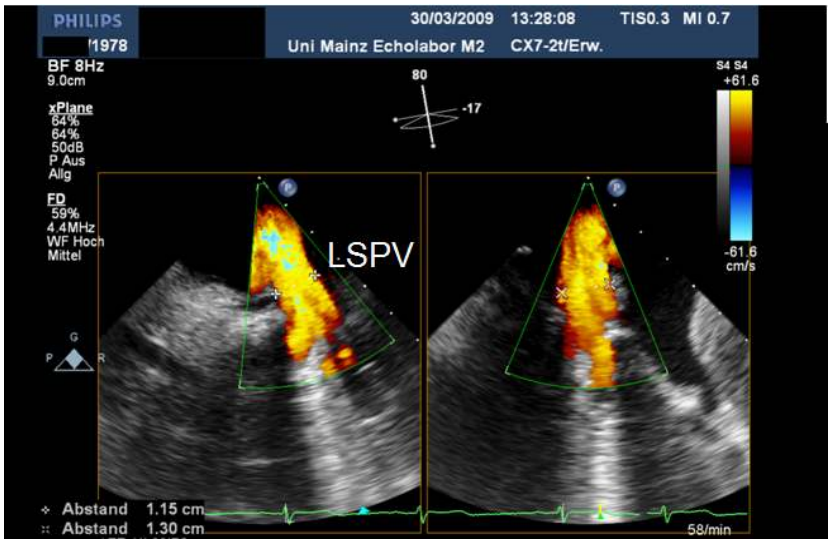

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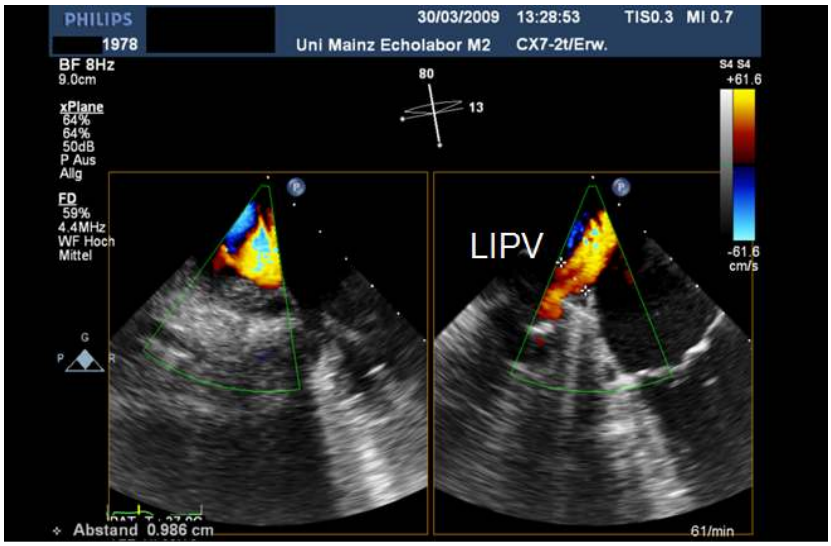


(D)

Fig. 1. Three-dimensional TEE-reconstruction of the left atrium providing an overview over the left-sided pulmonary veins and the left atrial appendage (a, b). Evaluation of the flow within the ostium of the LSPV (c) and the LIPV (d; 3D color Doppler datasets). The left pulmonary veins have separate ostia (rather close together) and there is no pulmonary vein stenosis

LAA = Left atrial appendage, LIPV = Left inferior pulmonary vein, LSPV = Left superior pulmonary vein, MV = Mitral valve, TEE = Transesophageal echocardiography

A linear lesion at the LA roof could be created successfully in seven patients in this group (7/7 patients). In addition, a continuous linear lesion was created at the mitral isthmus in 2 patients (10%) in group B. A mitral isthmus ablation was only performed in patients with spontaneously occuring or inducible left atrial isthmus-dependent flutter.

Successful catheter ablation of the right atrial isthmus was performed in a total of 7 patients (group A1: 4 patients, group A2: 1 patient, group B: 2 patients). Catheter ablation of the cavotricuspid isthmus was only performed in patients with spontaneously occuring or inducible typical atrial flutter.

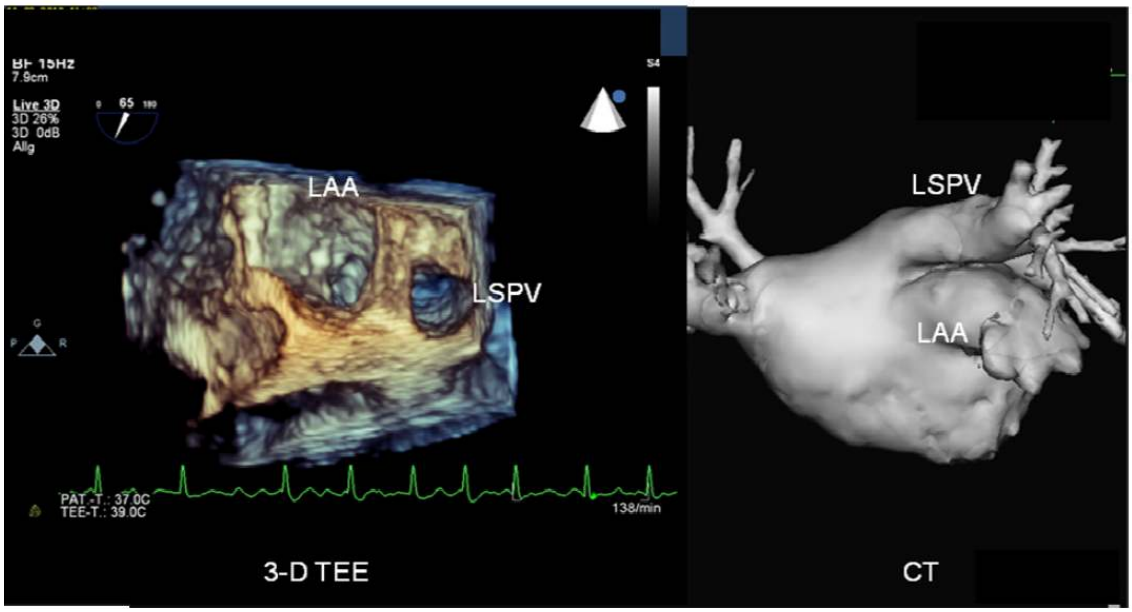
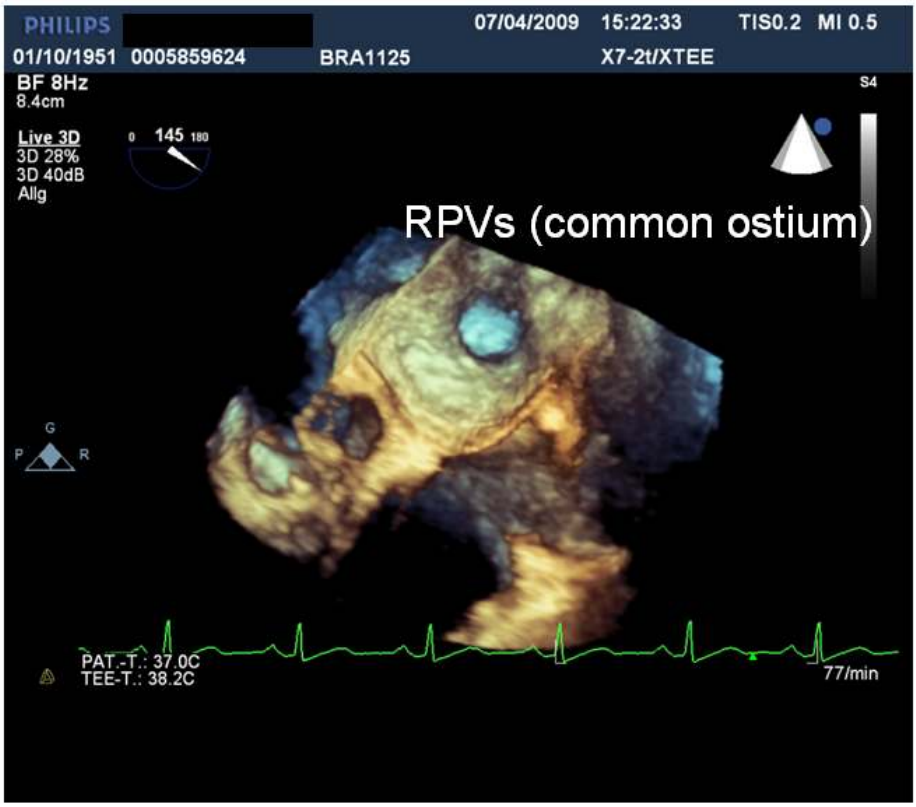


Fig. 2. Three-dimensional TEE-reconstruction (a) and 3D MDCT-reconstruction (b) providing an overview over the left atrial anatomy. Note the large left atrial appendage (LAA) and its close anatomical relationship to the left superior pulmonary vein (LSPV)

CT = Computed tomography



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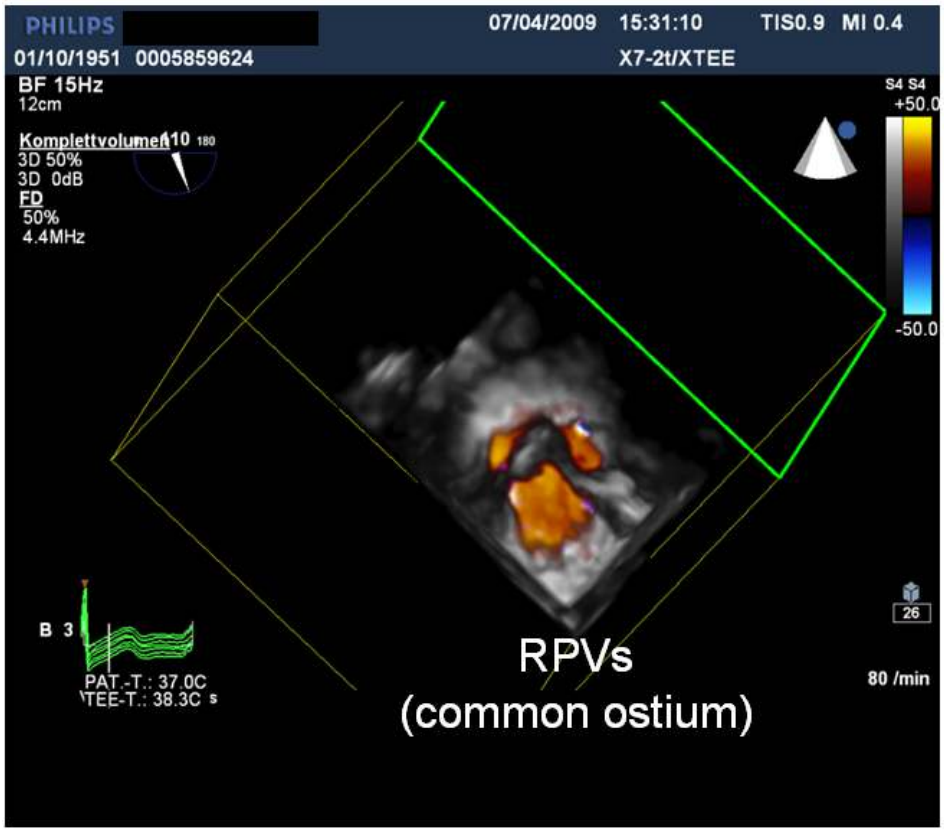

(B)

Fig. 3. Three-dimensional TEE-reconstruction (a) and 3D color Doppler dataset (b) revealing a common ostium of the right pulmonary veins (RPVs)

There were no major complications (e.g. cardiac tamponade, transient ischemic attacks (TIAs) or stroke, significant pulmonary vein stenosis (≥ 70%), periprocedural death) during the procedure in both groups.

3.3 Clinical Outcome

The mean follow-up was 795 days (SD ± 423 days) in group A and 966 days (SD ± 208 days) in group B (P = 0.1). The mean overall follow-up was 864 days (SD ± 360 days). All patients were enrolled in the clinical outcome analysis even if the PVs could not be visualized appropriately by 3D TEE.

Twelve months after the ablation procedure, 86.7% of the patients in group A (26 / 30; A1: 90.6% (10 / 11) / A2: 84.2% (16 / 19)) and 75.0% of the patients in group B (15 / 20) were free from an arrhythmia recurrence (P = 0.82; in total: 41 / 50 patients (82.0%)). Two years after the procedure, the overall success rate was 76% (no arrhythmia recurrence in 38 out of 50 patients). Twenty-four out of 30 patients in group A (80.0%; A1: 81.8% (9 / 11 patients) / A2: 78.9 % (15 / 19 patients)) and 14 out of 20 patients in group B (70.0%) were still free from an arrhythmia recurrence (P = 0.75).

According to the analysis of the questionnaire, 39 / 50 patients (78%) were completely asymptomatic at 24-month follow-up.

There were no major complications during or after the ablation procedures (including a follow-up duration of 24 months). Minor complications were observed in 9 patients (group: A1 / A2 / B: 2 / 1 / 5 patients; groin hematoma: 3 patients, pulmonary vein stenosis 30-70%: 0 patients, noninfectious pericarditis: 3 patients, minor pericardial effusion: 1 patient, hyperthyroidism: 1 patient, residual defect of the atrial septum: 1 patient).

Analysing the clinical course of the patients who experienced an arrhythmia recurrence during

follow-up, 7-day Holter monitoring revealed paroxysmal atrial fibrillation in 9 patients (group A: 7 patients (A1: 6 / A2: 1); group B: 2 patients) and persistent atrial fibrillation in 3 patients (group A: 2 patients (A1: 1 / A2: 1); group B: 1 patients). No modification of the antiarrhythmic medication and no repeat ablation procedure was required in 3 patients (group A1/A2/B: 1/0/2 patients) with an arrhythmia recurrence because they were almost asymptomatic. In 3 patients (group A1/A2/B: 1/0/2) with a symptomatic arrhythmia recurrence symptoms could be controlled by modifying the antiarrhythmic drug therapy or an electrical cardioversion. Six patients with symptomatic arrhythmia recurrences had to undergo another ablation procedure (group A1/A2/B: 0 / 4 / 2 patients).

Three months after the ablation procedure, all antiarrhythmic drugs (except for beta-blockers) were discontinued in all but 5 patients. Two patients remained on a class III antiarrhythmic drug (amiodarone: group A1/A2/B: 1/0/1) and three patients continued to take a class Ic antiarrhythmic drug (flecainide: 1/1/1).

3.4 Cardiac Imaging

A 3D TEE could be performed successfully in all patients immediately prior to the ablation procedure (only in 2 patients the TEE probe was left in place during the entire ablation procedure for real time monitoring of the intervention). All PV ostia could be evaluated in 42 / 50 patients (84%; group A1/A2/B: 8/16/18 patients). In 8 patients (group A1/A2/B: 3/3/2), the right PVs could not be evaluated (RSPV: 0 patients; RIPV: 2 patients; RSPV+RIPV: 6 patients). The left-sided PVs could not be evaluated in 5/50 patients (group A1/A2/B: 3/0/2 patients). In all of these patients, both left-sided PVs (and the right-sided PVs) could not be evaluated. The image quality was good in 42/50 patients (84%; i.e. all PV ostia could be visualized precisely). In 5 / 50 patients, the image quality was moderate (10%). Only poor image quality could be obtained in 3/50 patients (6%). The grading "poor image quality" was used when the PVs could hardly be visualized. Poor image quality was mostly due to the fact that the right-sided PVs were difficult to visualize.

Poor or insufficient image quality was mostly due to anatomical reasons. The underlying rhythm did not influence the image quality very much and the image quality was acceptable even if AF with rapid ventricular response was present during the examination in most cases.

In all patients, a 3D TEE-reconstruction of the left atrium could be generated. These 3D reconstructions were displayed in a synchronised way during the ablation procedure. The 3D TEE - models provided an excellent overview over the anatomy of the left atrium in all cases. They revealed a high degree of variability with regard to the individual anatomy. There was a large left atrial appendage in 2 patients (group A: 1, group B: 1). The distance between the left atrial appendage and the left superior pulmonary vein was extremely short (< 5 mm (measured on the 3D-TEE models)) in 3 patients resulting in a difficult ablation procedure (group A1/A2/B: 1 / 1 / 1 patients).

The 3D reconstructions did also provide valuable information about the anatomy of the pulmonary veins (see Table 2). They provided a good overview over the anatomy of the pulmonary veins similar to standard CT or MRI scans. In 2 patients, there was a common ostium of the left-sided (n = 1) or right-sided pulmonary veins (n = 1). There was an accessory pulmonary vein in 1 patient (right: 1, left: 0). The TEE findings concerning the anatomy of the pulmonary veins were confirmed by invasive pulmonary vein angiography (biplane) in all cases. In addition, invasive pulmonary vein angiography revealed a branching of a pulmonary vein close to the orifice / LA-PV junction (within ≤ 0.5 cm from the ostium) in 3 patients (LSPV: 0, LIPV: 0, RSPV: 2, RIPV: 1), which could not be visualized by 3D TEE. The mean diameter of the main trunk of all pulmonary veins is given in Table 3 (as assessed by three-dimensional transesophageal echocardiography and invasive pulmonary vein angiography). There were no significant differences between the two techniques with regard to the estimated PV diameter (although the PV diameters determined by 3D TEE tended to be slightly smaller than those determined by invasive pulmonary vein angiography). In addition, the 3D TEE-reconstructions provided valuable information for planning linear lesions by providing an excellent overview over the individual left atrial and PV morphology.

In summary, these 3D TEE-reconstructions provide detailed knowledge of the individual left atrial and PV morphology thereby facilitating the ablation procedure. The ablation procedures were strongly influenced by the use of the 3D

reconstructions. In group A, the information derived from the 3D TEE-reconstructions was valuable to decide whether the patients were scheduled for radiofrequency catheter ablation or for a cryoablation procedure. In 1 patient in group A, we refrained from using the cryoballoon technique because of an unfavourable PV anatomy (common PV ostium).

The knowledge of the individual left atrial and PV morphology had direct implications for the ablation strategy. Thereby, typical pitfalls were revealed which are associated with a high risk of serious complications such as pulmonary vein stenosis. In 2 patients (group A: 1 patient, group B: 1 patient) we refrained from isolating one (1 patient) or two (1 patient) pulmonary veins because of an unfavourable pulmonary vein morphology (e.g. small diameter, endangered side branches or a pre-existing moderate stenosis (n = 1)).

Additionally, an incomplete PV isolation was accepted in 3 patients (group A: 1 patient, group B: 2 patients; one PV: 3 patients, two PVs: 0 patients). An incomplete PV isolation was accepted in 2 patients in group B because of a small distance between the LAA and side branches of the left superior pulmonary vein. In one patient in group A2, an incomplete isolation of a small right inferior pulmonary vein was accepted. This PV could not be isolated completely with the first gerneration cryoballoon because of an atypical drainage pattern (very inferior) and an unfavourable relationship to the transseptal access. Furthermore, an incomplete isolation of an accessory PV was accepted in 1 patient.

In patients undergoing a cryoballoon procedure, the 3-D TEE reconstructions were very helpful for chosing the initial balloon diameter. Furthermore, they were helpful to decide whether to use a cryoballoon with a different diameter or a standard cryoablation catheter in case of incomplete PV isolation after several cryoapplicatons with the type of cryoballoon chosen at the beginning of the procedure.

In addition, three-dimensional transesophageal echocardiography was used for visualization of the cryoballoon and the circular mapping catheter during the ablation procedure in 2 patients (see Fig. 4). Thereby, an excellent overview could be obtained concerning the position of the catheters and their anatomical relationship to the relevant left atrial structures.

4. DISCUSSION

Catheter ablation has become an important therapeutic option for patients with highly symptomatic and drug-refractory atrial fibrillation. Nevertheless, catheter ablation of atrial fibrillation is still a challenge. This is partially due to the high degree of variability with regard to the individual anatomy. Therefore, 3D imaging systems (MRI and MDCT) are frequently used prior to an ablation procedure. They provide detailed information about the individual left atrial anatomy, thereby facilitating the ablation procedure. However, these imaging techniques are associated with significant limitations (e.g. radiation exposure (MDCT), inappropriate image quality in the presence of atrial fibrillation with rapid atrioventricular nodal conduction (especially MRI), additional costs).

Therefore, we have evaluated the usefulness of three-dimensional transesophageal echocardio-graphy for assessing the left atrial anatomy prior to catheter ablation of atrial fibrillation (either by radiofrequency catheter ablation or by cryoablation). There is only few data about the usefulness of 3D transesophageal echocardiography in the electrophysiology laboratory [25,27] and no sufficient data concerning 3D TEE for preprocedural imaging prior to catheter abklation of AF.

4.1 Main Results

Catheter ablation of paroxysmal atrial fibrillation could be performed successfully in 11 patients in group A using radiofrequency catheter ablation (group A1) and in 19 patients using cryoablation (group A2) based on prior 3D TEE imaging. In group B, catheter ablation of persistent atrial fibrillation could be performed successfully in 20/20 patients using radiofrequency catheter ablation and a basically circumferential ablation strategy.

Two years after the ablation procedure, 80.0% of all patients in group A (24 / 30) were still free from an arrhythmia recurrence compared to 70% of patients in group B (14 / 20; P = 0.75). The overall success rate was 76% at 24-month follow-up. There were no major complications during or after the ablation procedures in both groups.

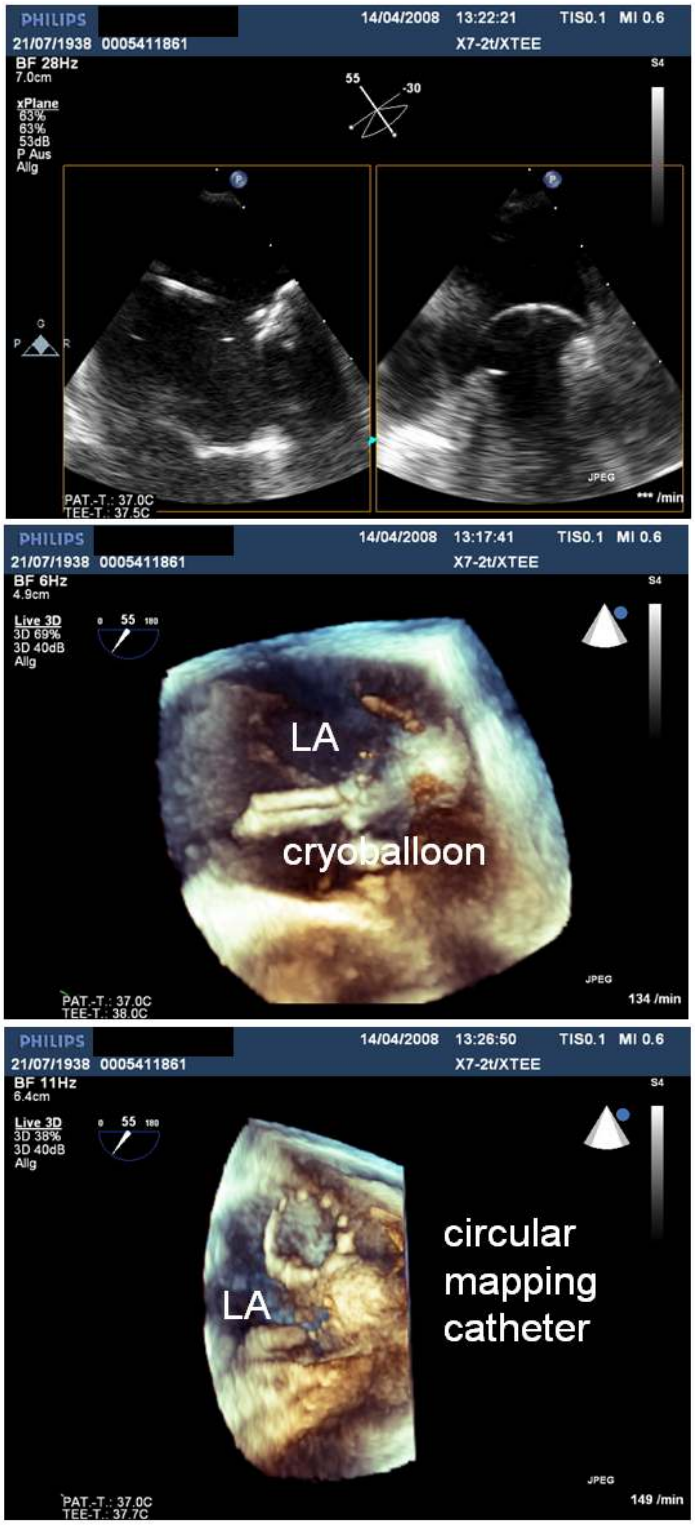

Fig. 4. Cryoablation of atrial fibrillation: Visualization of the cryoballoon (Arctic Front; Medtronic) and the circular mapping catheter (Lasso 2515; Biosense Webster) during the ablation procedure by three-dimensional transesophageal echocardiography

LA = Left atrium

Three-dimensional transesophageal echocardiography could be performed successfully in all patients prior to the ablation procedure. All pulmonary vein ostia could be evaluated in 42/50 patients (84%). The image quality was good in the majority of cases and several variations of the left atrial anatomy could be visualized precisely. The image quality was acceptable even if AF with rapid ventricular response was present during the examination and the TEE findings correlated well with the PV angiographies performed during the ablation procedure.

However, invasive pulmonary vein angiography was superior to 3D TEE with regard to the detection of side branches close to the pulmonary vein ostium. Although the pulmonary vein diameter determined by 3D TEE tended to be slightly smaller than the values obtained by invasive pulmonary vein angiography this was not statistically significant. However, a future study with a larger patient cohort is needed to rule out a possible underestimation of the PV diameter by 3D TEE.

The results of our study demonstrate that catheter ablation of atrial fibrillation can be performed safely and effectively using radiofrequency catheter ablation or cryoablation after pre-procedural 3D TEE imaging. Three-dimensional transesophageal echocardiography overcomes most of the limitations of other imaging techniques (CT/MRI) frequently used for evaluation of the PV anatomy (such as radiation exposure and inappropriate image quality in the presence of atrial fibrillation with rapid atrioventricular nodal conduction). A TEE should be performed prior to an AF ablation procedure to rule out the presence of a left atrial thrombus in all patients anyway. Thus, a 3D TEE does not result in additional patient discomfort or cost and is less time-consuming than other techniques (average time needed for 3D TEE data acquisition: 2-3 minutes). This suggests that 3D TEE might be the preferred imaging technique for analysing the left atrial anatomy prior to an ablation procedure in the future. By using 3D TEE the radiation exposure for preprocedural imaging can be reduced to zero and the costs can be reduced significantly depending on the technical resources of the institution as well as the national healthcare system.

It should be added that most of the quantative data. (e.g. pulmonary vein diameter) can also be revealed by two-dimensional TEE. However, the opportunity of generating three-dimensional reconstructions of the left atrial anatomy gives the operator a more vivid impression of the individual LA morphology (comparable to MRI or MDCT reconstructions).

Furthermore, 3D TEE might be an interesting technique for monitoring the movement of the catheters during an ablation procedure (see Fig. 4). However, this is limited by the fact that deep sedation is required when the TEE probe remains in place for the entire procedure. Moreover, there might be an increased risk of esophageal injury (especially during RF ablation procedures).

5. LIMITATIONS

This is a feasibility study analysing our preliminary experience with catheter ablation of AF facilitated by the use of 3D TEE-reconstructions. The aim of this study was to show the usefulness of 3D TEE for PV visualization prior to an ablation procedure. The study was not primarily designed to prove that this technique is equivalent to or superior to other imaging techniques (MDCT, MRI or intracardiac ultrasound). Therefore, no comparison to MDCT or MRI data is provided. Obviously, the results of this study have to be confirmed by a future study with a larger patient cohort and a direct comparison to MDCT or MRI scans. Morover, a detailed intra- and inter-examiner variability analysis concerning the echo examinations must be performed in a future study with a larger patient cohort.

Furthermore, there are some technical limitations of 3D transesophageal echocardiography: first, the right pulmonary veins are sometines difficult to visualize. It should be pointed out that all pulmonary veins could be evaluated in only 84% of patients. In the remaining patients the operator has to rely on the invasive pulmonary vein angiography or use a different imaging technique (such as MRI, MDCT or intracardiac ultrasound). Second, the 3D TEE images can only be displayed in a manually-guided synchronized way during the ablation procedure on separate screens. No direct image fusion with the geometry created with a 3D mapping system (CARTO (Biosense Webster) or Navx/Ensite (St. Jude Medical, Saint Paul, MN, USA)) is available so far. Some technical modifications are needed to achieve this and the accuracy of these 3D reconstructions remains to be evaluated in future studies.

6. CONCLUSIONS

Catheter ablation of atrial fibrillation can be performed safely and effectively based on prior 3D TEE imaging. Three-dimensional TEE-reconstructions provide an excellent overview over the individual left atrial and pulmonary vein morphology, thereby facilitating the procedure. Typical pitfalls (e.g. complex pulmonary vein morphology, varying distance between the LAA and the LSPV) can be revealed and the ablation strategy can be modified appropriately to avoid serious complications.

Therefore, 3D TEE reconstructions might be of growing importance for catheter ablation of AF in the future. However, future randomized studies are needed to prove that this approach is superior to standard ablation procedures (e.g. using 3D MRI- / MDCT-reconstructions) with regard to success rates, complication rates and other parameters (e.g. radiation exposure).

CONSENT

As per international standard or university standard, patient's written consent has been collected and preserved by the authors.

COMPLIANCE WITH ETHICAL STANDARDS

All procedures were performed in accordance with the ethical standards of the responsible research committee, national law and with the 1964 Helsinki declaration and its later amendments. All procedures were performed as clinically indicated and informed consent was obtained from all patients. The study comprised a retrospective analysis of data obtained from clinically indicated routine procedures.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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