Pulmonary Vein Diameter Reduction After Radiofrequency Catheter Ablation for Paroxysmal Atrial Fibrillation Evaluated by Contrast-Enhanced Three-Dimensional Magnetic Resonance Imaging

Thorsten Dill, MD; Thomas Neumann, MD; Okan Ekinci, MD; Christiane Breidenbach, MD; Anna John, MD; Ali Erdogan, MD; Georg Bachmann, MD; Christian W. Hamm, MD, FESC; Heinz-F. Pitschner, MD, FESC

Background—Radiofrequency catheter ablation (RFCA) is a promising intervention to treat atrial fibrillation. However, pulmonary vein (PV) stenosis after RFCA has been reported. The aim of this study was to investigate the incidence and time course of pulmonary vein stenosis after RFCA within a period of 3 months. Contrast-enhanced magnetic resonance angiography (MRA) was used to visualize pulmonary veins and was compared with radiographic angiography.

Methods and Results—Forty-six consecutive patients with symptomatic paroxysmal atrial fibrillation had RFCA in the orifice of 138 pulmonary veins. Comparison of diameters measured in 44 untreated vessels either by radiographic angiography or with MRA established the reliability of MRA (r=0.934). MRA measurements revealed an incidence of relevant diameter reductions of ≥25% or stenosis of ≥50% after RFCA of 25 of 138 (18.1%) treated vessels 1 day and/or 3 months after ablation. A progression of diameter reduction after RFCA was observed in 8.3% (maximum 75%), whereas a regression was observed in 6.3% of treated PVs. Ablation at a radial angle of ≥180° of a pulmonary vein orifice increased the risk of diameter reduction significantly compared with ablation at a radial angle ≤180° (P=0.002).

Conclusions—The occurrence and progression of PV stenosis is a potential significant complication of RFCA in the orifice of pulmonary veins. These findings may have an impact on the technical performance of this intervention. In addition, long-term studies will be necessary to evaluate lumen reduction over time. MRA is a noninvasive, reproducible imaging modality for this purpose. (Circulation. 2003;107:845-850.)

Key Words: magnetic resonance imaging catheter ablation veins fibrillation

In patients with paroxysmal lone atrial fibrillation (AF) or mild cardiovascular disease, the most frequent origin of focal AF is situated within the pulmonary veins (PV). The reported results of radiofrequency catheter ablation (RFCA) of arrhythmogenic atrial myofibrils crossing into PVs are promising.1-5 Assessment of the pulmonary vein (PV) anatomy and dimensions before RFCA and during follow-up improves the evaluation of this new technique.

PV stenosis is a possible procedure-related complication1-5,6 that can progress to complete occlusion of a PV with severe and potentially life-threatening symptoms of segmental pulmonary hypertension. The incidence and time course of severe PV stenosis after RFCA is unclear at present. Repeat magnetic resonance angiography (MRA) of the PVs may be used without exposing the patient to the risks of repeat radiographic angiography and the additional discomfort of an invasive procedure.

The aim of this study was to detect and assess PV stenoses over time after RFCA with regard to different radial angles of energy delivery (<90°, ≥180°, >180°) as an early or late complication and to test MRA as an alternative imaging modality compared with standard radiographic angiography.

Methods

Study Population

Between April 2000 and August 2001, we prospectively studied 46 consecutive patients (52±10 years, 32 men) with highly symptomatic paroxysmal atrial fibrillation (PAF) refractory to ≥3 antiarrhythmic drugs, including class-I agents, β-blockers, sotalol, and amiodarone. PAF occurred 42±34 times within the last 3 months before the procedure. The mean duration of PAF before the ablation procedure was 14.4±14.1 hours. Symptomatic AF first occurred 8.9±6.1 years before enrollment in the study. Twenty-six patients had lone atrial fibrillation and 20 patients had mild heart disease,

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From the Department of Cardiology (T.D., T.N., O.E., C.B., A.E., C.W.H., H.-F.P.), Kerckhoff Heart Center, Bad Nauheim, Germany; the Department of Radiology (G.B.), Kerckhoff Heart Center, Bad Nauheim, Germany; and the Department of Cardiac MRI (A.J.), Royal Brompton Hospital, London, UK.

Correspondence to Thorsten Dill, MD, Kerckhoff Heart Center, Department of Cardiology/Cardiac MRI, Benekestrasse 2-8, 61231 Bad Nauheim, Germany. E-mail thorsten.dill@kerckhoff.med.uni-giessen.de

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including hypertensive cardiomyopathy or coronary artery disease with normal ejection fraction and normal atrial dimensions.

All patients gave written informed consent to the electrophysiological study and MRI.

**Electrophysiological Study**

All patients were studied after placement of 2 transseptal 8F sheaths in the left atrium by transfemoral venous access. One sheath was used to introduce a multipolar mapping catheter (Biosense Webster Lasso, 10 polar) into the PVs for mapping purposes. The second was used for the ablation catheter. A third 4-polar steerable catheter was placed in the lateral coronary sinus to apply the necessary extrastimuli. The ablation catheter was positioned on the angiographically identified atrial site of the PV ostium, proximal of the electrodes that record the input.

Only patients with a potential focus as a possible trigger of AF in at least one PV underwent ablation. The following deformations of the bipolar atrial signals were defined as suspicious for a PV myofibril signal: a fractionated signal with high-frequency components in sinus rhythm or induced by a single atrial extrastimulus delivered in the lateral coronary sinus, or spontaneous extrasystoles with fragmentation of the a wave in the PV orifice or distal from the PV orifice. The aim of the chosen ablation strategies was the electrical disconnection of the PVs and the left atrium. The procedure was successful when pacing near the PV ostial site could not penetrate into the PV or isolated spontaneous activity in the PV was not conducted to the atrial site.

To provide a systematic approach, the following ablation strategies were differentiated: (1) type A (TA), radiofrequency energy delivery at one spot or on an estimated radial angle of <90° within the orifice circumference of the PV; (2) type B (TB), radiofrequency energy delivery within the orifice of the PV on an estimated radial angle ≤180° of the total circumference; and (3) type C (TC), radiofrequency application of >180° of the PV circumference (Figure 1). Radiofrequency energy was delivered at the PV ostium with a power output of 15 to 50 W for 40 to 60 seconds. All ablations were carried out with the use of a cooled tip catheter (Chilli, 7F, Boston Scientific). Applied power during ablation was regulated to achieve a temperature at the electrode tip between 24°C and 30°C. Energy delivery was interrupted if temperature measurement on the catheter tip showed more than 30°C. Mean power and cumulative energy for each PV and for the different techniques (TA, TB, and TC) were registered.

**Radiographic Angiography of PVs**

In all patients, a conventional radiographic angiography of the target PV was performed by a power injection of 20 mL of a contrast agent (Imeron, 350 mg iodine/mL, Byk Gulden) before and after RFCA (Figure 2). The fluoroscopy images were stored on CD. Forty-five PVs with excellent contrast density before RFCA were used for diameter measurements with a quantitative coronary analysis program (Quantcor, Siemens). In this subgroup, vessel diameters as measured by quantitative coronary analysis in selective PV angiography were compared with MRA diameter measurements of the corresponding PVs.

**MRI Protocol**

For MRI, the patient was positioned supine in a 1.5-T scanner (SONATA, Siemens), and a phased-array radiofrequency coil was placed on the chest for imaging. Image acquisition was gated to the
ECG and was performed during breath-hold for ∼10 seconds. After the correct image planes were defined, fast precession steady-state sequence (True FISP)-cine images (TR, 32 ms; TE, 1.6 ms; SLT, 5 mm) were obtained for functional and anatomic evaluation in long-axis views (2- and 4-chamber views) and in selected planes adjusted to the individual course of the PV.

For 3D-MRA data acquisition and further image processing, a contrast-enhanced, nongated FISP-3D sequence (effective SLT typically ≤2 mm; slab thickness, 80 mm; FOV, 280×320 mm; matrix, 160×256; pixel size, 1.75×1.25 mm) was positioned in a paracoronary orientation, and after injection of contrast agent (0.1 mmol/kg body wt, Magnevist, Gd-DTPA, Schering), two consecutive breath-hold measurements were obtained.

In every patient, all PVs were imaged. Morphology and diameter of the proximal 20 mm distal to the ostium were evaluated by means of a multiplanar reconstruction algorithm (Figure 3).

Morphological findings and the applied different radial angles of energy delivery during RFCA for each PV were evaluated for correlations. A diameter reduction of ≥25% to <50% was interpreted as a relevant diameter reduction (DR). A diameter reduction of ≥50% was defined as a stenosis.

Each patient’s set of MRA scans and PV angiography were presented in random order to two different investigators who were unaware of the patient’s identity and the location of RFCA.

Reproducibility of MRA measurements was tested by comparing the diameter of untreated PVs at different time points.

### Statistical Analysis

Results are presented as mean ±1 SD for continuous variables and as percentages for categoric data.

Paired and unpaired t tests were used to compare repeated measurements and to compare measurements in different treatment groups. Differences between discrete variables were assessed by using the χ² test and Fisher’s exact test where necessary. Linear regression analysis was performed where appropriate. Independent predictors for the occurrence of a PV DR or stenosis were assessed by using multiple logistic regression analysis.

### Results

A total of 46 patients admitted to our institution for RFCA of AF were studied; 38 patients (83%) completed a follow-up of 3 months. All magnetic resonance scans were performed without complications. The average imaging time was 11.5 minutes per patient.

A total of 184 PV were evaluated; RFCA was performed in 138 of these. Final magnetic resonance evaluation at 3 months’ follow-up was done in 111 treated vessels (80%). In 6 patients, no follow-up MRA could be performed because of severe claustrophobia (1 patient), death of noncardiac cause (1 patient), interim pacer implantation (2 patients), and refusal (2 patients).

The Table shows the distribution of the applied RFCA technique for each of the 138 treated PVs.

### Comparison of MRA and Radiographic Angiography

For validation of MRA, vessel diameters measured on MRA were compared with those derived from radiographic angiography in a subset of 44 PVs. The correlation coefficient was calculated at 0.934 (P<0.001) (Figure 4).

For internal standardization and reproducibility testing of MRA measurements, diameters of all vessels not treated were compared before, 1 day after, and 3 months after RFCA. No significant change in diameter was noted (14.4±2.9 mm, 14.6±3.0 mm, and 14.5±2.9 mm, respectively, P=0.94).

### MRA Measurements

The mean diameter of all treated PVs was 15.2±2.4 mm before RFCA, 14.2±2.9 mm 1 day after RFCA (DR=7±16%), and 13.8±3.2 mm at 3-month follow-up (DR=9±21%).

Regarding anatomic positions of treated PVs before, 1 day after, and 3 months after RFCA, the diameters of the left upper PV (LUPV) (n=44, after 3 months n=36) were 15.4±2.5 mm, 14.1±2.9 mm (DR 8%, P=0.004), and
13.5±3.8 mm (DR 12%, \( P=0.006 \)), respectively. The corresponding values for the left lower PV (LLPV) (n=35, after 3 months n=28) were 14.2±2.4 mm, 12.6±3.5 mm (DR 11%, \( P=0.002 \)), and 12.6±3.4 mm (DR 11%, \( P=0.02 \)), respectively; for the septal upper PVs (SUPV) (n=40, after 3 months n=34) 16.1±2.3 mm, 15.3±2.2 mm (DR 4%, \( P=0.021 \)), and 14.9±2.4 mm (DR 5%, \( P=0.019 \)); for the septal lower PVs (SLPV) (n=19, after 3 months n=13) 15.0±1.7 mm, 14.9±1.8 mm (DR 0%), 14.5±1.7 (DR 3%, \( P=0.2 \)), respectively (Figure 5).

A total of 24 PVs (17%) had either a DR or a stenosis on day 1 and/or after 3 months. On day 1, 14 PVs (10%) showed a DR and 4 PV (3%) a stenosis. After 3 months, a DR was present in 10 PVs (7%) and a stenosis in 6 PVs (4%).

A DR was located on day 1/after 3 months in the LUPV in 1 of 3, in the LLPV in 3 of 2, and in the SUPV in 0/1.

For these PVs, total percent reduction was on day 1 33±15%, compared with 40±24% after 3 months.

In 26 treated PVs, a small increase of diameter (range, 6% to 18%) compared with baseline was measured.

**Figure 4**. Correlation of PV diameter measurements between MRI and radiographic angiography.

**Figure 5**. Time course of diameter changes for the different treated PVs (LUPV, LLPV, SUPV, and SLPV). A, Before RFCA; B, 1 day after; and C, after 3 months.

**Time Course of Diameter Changes After RFCA**

The intra-individual comparison of lumen changes revealed that 4 patients had complete reversal of diameter reduction in 8 (5.8%) treated PVs (2 stenoses, 6 DR), comparing the measurement on day 1 and after 3 months.

Five patients (6 PVs, 4.3%) with no DR or stenosis at day 1 after treatment had DR (n=5) or stenosis (n=1) at 3 months.

In 4 patients with DR or stenosis at day 1 (range, 27% to 58%) and a 3-month control, a progressive DR/stenosis (range, 53% to 75%) was detected in 4 (2.9%) PVs.

Overall, a reversal of DR/stenosis occurred in 8 (5.8%) PVs. In contrast, progressive DR/stenosis was present in 10 (7.2%) PVs. In one patient, a pseudo-occlusion of the LUPV occurred 3 months after PVI. At that time, a perfusion defect was present in the left upper pulmonary lobe proven by scintigraphy. However, a pulmonary embolus was seen in the upper segmental branch of the left pulmonary artery. The patient had exertional coughing and dyspnea as a result of pulmonary embolism. After lysis of the embolus, the same PV diameter was found as before treatment. All other patients with DR/stenosis were free of clinical symptoms.

**Applied RFCA Technique and Occurrence of DR or ST**

The different radial angles of energy delivery applied in different PVs are depicted in the Table. The recorded energy data are as follows: Cumulative energy in LUPV was 17,247±1005 J; in LLPV, 11,216±676 J; in SUPV, 14,767±1030 J; and in SLPV, 9,994±1091 J, respectively. The difference is statistically significant (\( P<0.0001 \)). The mean power applied was in LUPV, 36.65±10.14 W; in LLPV, 33.80±9.85 W; and in SUPV, 35.13±11.0 W; and in SLPV, 28.30±13.20 W (\( P=0.02 \)). The cumulative energy applied with the different techniques was for TA 7910 J ±6234 J; for TB, 13,689±10199 J; and for TC, 17,579±10634 J (\( P<0.001 \)).

The mean power applied with the different techniques was for TA, 27.04±12.64 W; for TB, 33.12±10.70 W; and for TC, 36.94±9.80 W (\( P=0.0003 \)).

In 95.7% (132 of 138) of the ablated pulmonary veins, we achieved a complete disconnection of the PV and the left atrium.

DR/stenosis at any time after procedure TA, TB, and TC occurred in 11% (5/46), 11% (1/9), and 22% (18/83), respectively. Stenosis was observed only after procedure TC and occurred in 8% (7/83). The diameter reduction after procedure TC at day 1 was significantly larger than after procedure TA and TB (41±12%, n=15 versus 30±5%, n=3 FA, \( P=0.002 \); Figure 6), respectively. In PVs with progressive DR/stenosis, procedure TC was performed in 70% (7/10), procedure TA in 20% (2/10), and TB in 10% (1/10).
Some authors have reported the occurrence of severe PV stenosis immediately or within a few days after RFCA.\textsuperscript{2,13–15} However, late occurrence after some weeks or months has also been reported.\textsuperscript{15–19} In this study, a delayed progression of DR/stenosis has been detected in 8.3%. These observations support the assumption that progression of early stenosis without clinical symptoms or of DR to a severe stenosis causing clinical symptoms (eg, severe segmental pulmonary hypertension) may occur and emphasize the necessity of follow-up investigations.

Histologic findings in a dog model after RFCA within the PVs have been described in detail by Taylor et al.\textsuperscript{20} They reported severe stenosis and occlusions of PV after extensive RFCA within the PV in 9 treated mongrel dogs. Luminal narrowing was observed in 22 of 33 pulmonary veins in which radiofrequency energy was applied. They found endovascular contraction and proliferation of elastic lamina in combination with chronic inflammatory cell activity surrounding the vessel, resulting in progressive PV stenosis. The observed regression in 6.3% of treated PVs in our study might be caused by reversible acute edema.

The occurrence of acute and progressive DR/stenosis was clearly related to the applied different angles of energy delivery at the PV ostia during RFCA, as demonstrated above. Ablation with a radial angle $>180^\circ$ (TC) required a significantly larger amount of delivered radiofrequency energy than ablation with a radial angle $\leq180^\circ$ (TB) or $<90^\circ$ (TA). On the one hand, energy delivery with a radial angle $>180^\circ$ increased the clinical success rate in our cohort as well as in others.\textsuperscript{3} On the other hand, it appears to increase the risk for potential significant complications. This hypothesis is supported by the fact that in all PVs with stenosis in this study, a total radiofrequency energy amount of at least 25,000 J and a mean power of $>35$ W was applied, which was approximately one-third more compared with the average amount in other PVs. Additionally, most DR occurred in the LUPV, in which the highest mean power and cumulative energy was applied. According to the few available data in the literature based on single-case observations regarding applied power and energy, the maximum power should not exceed 30 to 35 W to avoid the development of DR or stenosis.\textsuperscript{5,6,19} The data of the present study support this recommendation, but the applied ablation technique also has influence on the development of DR or stenosis. Scheiman and Morady\textsuperscript{21} postulated that the best technique currently available for curing paroxysmal AF (assuming it originates from the PVs) is electrical isolation of the PVs by discrete applications of radiofrequency energy at the ostia, guided by pulmonary vein potentials. The usage of a nonfluoroscopic mapping system to stay away from the direct ostial site as proposed by Pappone et al\textsuperscript{22} may reduce the risk of DR or stenosis.

**Conclusions and Perspectives**

RFCA has been proven to be a successful modality to treat supraventricular tachycardias with a low risk profile. Increasing success rates have been reported for the treatment of PAF by RFCA of arrhythmogenic myofibrils entering the PVs in the human left atrium. However, the risk of severe compli-
cations appears to be higher compared with RFCA of other supraventricular tachycardias. Long-term studies with systematic follow-up are necessary to evaluate complications and especially to identify progressive diameter changes. MRI has not been proven that alternative energy sources such as cryocatheter ablation and ultrasound are superior to RFCA in the treatment of other supraventricular tachycardias. However, these alternative techniques may be of special interest for PVI.

Further investigations to determine the minimal amount and optimal location of radiofrequency energy application to achieve sufficient clinical success with a low risk for the development of DR/stenosis in PVs are needed. So far it has not been proven that alternative energy sources such as cryocatheter ablation and ultrasound are superior to RFCA in the treatment of other supraventricular tachycardias. However, these alternative techniques may be of special interest for PVI.

References

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