Neuropsychological decline after catheter ablation of atrial fibrillation

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BACKGROUND Cerebral embolic events represent recognized side effects after catheter ablation in the treatment of recurrent atrial fibrillation (AF).

OBJECTIVE The study was performed to analyze the neuropsychological outcome and to detect new embolic ischemic brain lesions after therapeutic left atrial catheter ablation of AF.

METHODS We enrolled 23 patients with recurrent AF who underwent elective circumferential pulmonary vein isolation. The primary endpoint was the neuropsychological outcome 3 months after intervention in contrast to the results of non-AF controls (n = 23) without ablation and in covariance of baseline performance. Cerebral diffusion-weighted magnetic resonance imaging (DWI) was performed in 21 AF patients at baseline, 2–4 days, and 3 months after intervention.

RESULTS In 3/21 patients (14.3%), new ischemic lesions were detected on DWI shortly after intervention. In one patient, a territorial middle cerebral artery infarct occurred with severe clinical symptoms. The other two patients represented clinically silent small lesions. In contrast to the control group and in covariance of baseline performance, the ablation group showed worse neuropsychological outcome in verbal memory (one of five cognitive domains) with an effect size of $d = 0.93[t\ (.05;\ 42) = -3.53;$ $P < .001$; false discovery rate $(\mathrm{FDR})_{crit} \leq .01]$.

CONCLUSION Adverse neuropsychological changes after left atrial catheter ablation are verifiable in verbal memory and, conjoined with ischemic brain lesions on DWI, might represent cerebral side effects of this procedure.

KEYWORDS Catheter ablation; Atrial fibrillation; Cognition; Diffusion weighted imaging; Stroke

ABBREVIATIONS **AF** = atrial fibrillation; **ANCOVA** = analysis of covariance; **DWI** = diffusion-weighted imaging; **FDR** = false discovery rate; **FOV** = field of view; **MES** = microembolic signal; **MRI** = magnetic resonance imaging; **PVI** = pulmonary vein isolation; **RF** = radiofrequency; **SD** = standard deviation; **SEM** = standard error of mean; **TEE** = transesophageal echocardiography; **TIA** = transient ischemic attack; **TSE** = turbo spin-echo

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Introduction

Catheter ablation is increasingly used and recommended as a second-line therapy to treat recurrent symptomatic atrial fibrillation (AF) in patients who remain refractory to conventional antiarrhythmic treatment.[1] The technique involves an electrical isolation of the pulmonary veins achieved by circumferential ablation. Transmural lesions are produced using radiofrequency (RF) energy to destroy myocardial sleeves extending into the pulmonary veins where AF is thought to originate.[2] New ablation techniques like cryoablation, using a liquid refrigerant that flows through a catheter to destroy selective tissue locations by freezing, were designed in the past years and showed reasonable success rates.[3]

Stroke, transient ischemic attacks (TIA), and other embolic events due to thrombogenicity of the procedure represent recognized side effects during and after left atrial catheter ablation.[4,5] The incidence of stroke varies between less than 1% and 7%.[6] According to a large multicenter study, ischemic brain lesion (and myocardial damage) was the third most frequent cause of death, after cardiac tamponade— including irreversible pump failure—and atrioesophageal fistulas.[7] Thrombus formation during and after catheter ablation might result from platelet and coagulation system activation either directly at the catheter material or at the site of endothelial application.[8,9] Cerebral complications, supposedly caused by cardiogenic embolism, were thus reported as intra-, peri-, or postprocedural strokes/TIA with manifest neurological symptoms.

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Transcranial Doppler monitoring of basal cerebral arteries indicates that several thousand microembolic signals (MES) can be detected within the basal cerebral arteries during the ablation process.[10] The microembolic load of patients undergoing AF ablation is therefore comparable to those subjected to major cardiac surgery (i.e., bypass surgery or valve replacement). Since cardiac surgery can cause long-lasting neuropsychological changes[11–13] and cerebral microembolization has been shown to play an important role in this context, the present study was conducted to evaluate whether left atrial ablation might lead to neuropsychological deficits similar to those after major cardiac surgery.

Materials and methods

Twenty-six consecutive AF patients undergoing elective left atrial catheter ablation by circumferential pulmonary vein isolation (PVI) were originally included in the study. At inclusion, a baseline neuropsychological assessment was performed. Inclusion criteria were recurrent symptomatic AF refractory to antiarrhythmic treatment, age >18 years, and German language. Exclusion criteria were previous cerebral brain damages (e.g., after stroke, traumatic injury) or presence of severe neurological/psychiatric disorders, previous ablation procedures or ablation procedure performed under general anesthesia, previous surgeries under cardiopulmonary bypass, and contraindication for magnetic resonance imaging (MRI) (e.g., metal, claustrophobia). Two (7.7%) of 26 AF patients fulfilled exclusion criteria and were accordingly excluded from further analysis. One patient (3.8%) refused the ablation procedure shortly before treatment. Twenty-three patients, who completed either MRI or cognitive assessment or both at all time points, were included in further analysis. Furthermore, 23 healthy volunteers—who were comparable regarding age, education, gender, and global medical characteristics (except for AF)—were enrolled with the same exclusion criteria (except for MRI contraindication) and completed cognitive examination at baseline and 3 months later. Volunteers were recruited mainly from staff, community facilities, and homes for the aged. All patients and healthy control clients signed informed consent.

Transesophageal echocardiography (TEE) was performed before the ablation procedure in patients who were not sufficiently anticoagulated or in those patients for whom anticoagulation was not documented adequately.

Procedures were performed in a fasting state under conscious sedation and analgesia with appropriate doses of midazolam and piritramid. After transseptal puncture, heparin was administered and infused to maintain an activated clotting time of $\geq$300 seconds. Measurements were performed every 30 minutes routinely. In addition, continuous infusions with heparinized saline by a rate of 180 mL/hour were connected to the transseptal sheaths to avoid clot formation or air embolism.

The left atrium was accessed via the transseptal route from the right femoral vein. In RF ablation, a steerable 8-Fr transseptal sheath (Agilis, St. Jude Medical, Eschborn, Germany) was used in addition to a second, nonsteerable 8-Fr sheath (SL1, St. Jude Medical). The RF-based circumferential isolation of pulmonary veins was performed using a 4-mm irrigated-tip catheter (Celsius Thermo-Cool, Biosense Webster, Diamond Bar, California, USA). The cutoff temperature of the generator was 42°C, and energy delivery was limited to a maximum of 35 W. Successful ablation was defined as complete elimination of all fragmented signals at the pulmonary vein ostium. Mapping was performed using either a 10-polar Lasso catheter (Biosense Webster) or a high-density mapping catheter (MESH, Bard Inc., Karlsruhe, Germany).

In cryoballoon ablation, a steerable 12-Fr sheath (FlexCath, CryoCath Medtronic, Meerbusch, Germany) was used to guide the cryoballoon catheter. As in RF ablation procedures, a second nonsteerable 8-Fr transseptal sheath was used to guide the mapping catheter. Cryocatheter ablation of pulmonary veins was performed using a 23 or 28 mm cryoballoon catheter (ArcticFront, CryoCath Medtronic). If necessary, a residual gap was closed using a large-tip cryocatheter FreezorMAX. Mapping of the PVs was performed by a suitable Lasso catheter. The cryoballoon ablation procedure is described in detail elsewhere.[3]

Complete isolation was verified as a reduction of all signals $\leq$0.2 mV. In sinus rhythm, exit block from the vein was confirmed by pacing at the location of bipolar signals within the pulmonary vein ostium in all patients. A 20-minute observation period was used after the isolation to check for possible recurrence of conduction.

During the ablation procedure, the majority of patients (81%) were in sinus rhythm and four patients (19%) were in AF. For postablation management, intravenous heparin was continued to achieve a partial thromboplastin time of 50–70 seconds. Between the postinterventional days 2 and 5, a 24- to 48-hour Holter electrocardiogram was obtained in every patient. Before hospital discharge, all patients underwent transthoracic echocardiography to exclude pericardial effusion. Oral anticoagulation with coumadin was started 1 day after PVI, targeting an international normalized ratio of 2.0–3.0 for at least 3 months. During a blanking period of 3 months, antiarrhythmic treatment was allowed even in asymptomatic patients to facilitate maintenance of sinus rhythm. Antiarrhythmic drugs were stopped after 3 months in the majority of patients. Antiarrhythmic drug therapy was continued only in patients with ongoing highly symptomatic episodes of AF beyond 3 months after intervention.

After discharge from the hospital, patients were scheduled for quarterly follow-up visits. Seven-day Holter electrocardiogram recordings were obtained at each follow-up visit. At 3 months of follow-up, neuropsychological assessment was repeated and compared with the baseline assessment. Overall, 30 patients receive AF ablations in this clinical center weekly, with a success rate of 72%.

Cerebral MRI was performed at baseline (1 week to 1 day before procedure), and 2–4 days and 3 months postablation, using a 1.5T device (SONATA; Siemens, Erlangen,