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Wide area left atrial appendage isolation for atrial fibrillation therapy: Long-term succes and incidence of stroke and thrombus formation

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Background: Pulmonary vein isolation (PVI) has evolved into an effective strategy for the treatment of atrial fibrillation (AF). Yet, stable sinus rhythm (SR) cannot be achieved by PVI alone in some patients (PVI non responder). Wide area left atrial appendage isolation (LAAI) has been suggested to maybe improve outcome in recurrent AF. Yet, this strategy may be associated with an increased risk of LAA-thrombus and subsequent embolic events. This study sought to assess the long-term success and the incidence of embolic events and LAA-thrombus formation after LAAI.
Methods: A total of 116 patients with radiofrequency (RF) based LAAI were prospectivly enrolled (LAAI group). LAAI was achieved after a mean of 2.1±1.1 previous procedures. Oral anticoagulation (OAC) independently of the individual CHA2DS2-VASc score was recommended to all patients. The patients were compared with matched patients with comparable baseline characteristics who underwent RF based AF ablation without LAAI (n=116 patients, control group). A transesophageal echocardiography was performed during follow-up in 95/116 (82%, LAAI) and 89/116 (77%, control) patients.
Results: During a follow-up period of 60 months 36.6% (LAAI) and 27.1% (control) of patients showed stable SR (p=0.0179). Embolic cerebrovascular events occurred in 17/116, 14.7% (LAAI) and 3/116, 2.6% patients (control, p=0.00147). LAA-thrombus was identified in 22/95, 23.2% (LAAI) and 2/89,2.2% patients (control, p<0.0001). LAA-closure was recommended to the LAAI patients and has been performed in 46/116 (39.7%) patients. Exept 1/46 patient (2.2%) with thrombus formation on the LAA-closure device no further thrombi of stroke occurred.
Conclusions: This prospective study showed that RF-based LAAI is able to improve long-term outcome of AF ablation procedures compared to a matched control group without LAAI. However, a high incidence of embolic stroke and TIA as well as LAA-thrombus formation was observed despite sufficient OAC. Therefore, LAA-isolation should be taken into consideration due to a moderate benefit and potential risk of embolic events. Furthermore LAA-clorsure should be considered in those patients to maybe prevent LAA-thrombi and embolic stroke.

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The impact of genetic mutations on ventricular tachycardia substrate types and ablation outcome in patients with non ischemic cardiomyopathy

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Background: There are limited data on the prevalence of genetic mutations associated with malignant ventricular tachycardia (VT) in patients with non-ischemic cardiomyopathy (NICM) referred for VT ablation. In addition, the impact of pathogenic mutations on the arrhythmogenic substrate localization and ablation outcome has not yet been investigated.
Methods: Eighty-nine patients (56±15years; 84% male, LV ejection fraction 38±13%) with NICM referred for ablation of recurrent sustained VT and a predominantly left sided arrhythmogenic substrate between 2008-2017 were included. All patients underwent electroanatomical voltage mapping (EAVM) and testing of 55 NICM-related genes using next generation sequencing. EAVM data were analyzed with regard to uni (<7.95mV) - and bipolar (<1.5mV) low-voltage areas with fragmented, double and late potentials in order to determine the scar-related substrate for VT. Patients were followed for VT recurrence and mortality. Patients with (likely) pathogenic mutations were compared to patients with either no mutations or with variants of unknown significance (VOUS).
Results: The prevalence of class 4/5 (likely pathogenic/pathogenic) mutations was 36% (N=32/89). The most frequent mutations were found in LMNA- [N=10, 11%], TTN- [N=4, 5%], PLN- [N=4, 5%], DSP-, ABCC9-, MYPH- and RBM20- [N=2 respectively, 2% each] genes. VOUS were identified in 19 patients (22%). Analysis of EAVM revealed two dominant scar patterns: anteroseptal in 50 patients (56%) and inferolateral in 39 patients (44%). Patients with a class 4/5 mutation had more often an anteroseptal scar pattern, N=25/32 (78%) vs. N=25/57 (44%) of patients without mutation/VOUS; P=0.002. After a median follow-up of 2.0 years (IQR 1.9-3.0), 51 (57%) patients experienced VT recurrence: 26/32 (81%) with a class 4/5 mutation vs. 25/57 (44%) without mutation/VOUS; P<0.001. Mortality was 27% (N=24) and was significantly higher in patients with a (likely) pathogenic mutation (N=16/32, 50%) vs. patients without mutation/VOUS (N=8/57, 14%); P<0.001. Multivariate analysis showed that presence of a (likely) pathogenic genetic mutation was associated with a decreased 2-year VT-free-survival (hazard ratio 1.7, CI 1.1-2.5, P=0.008).
Conclusions: In patients with NICM and recurrent VT a genetic cause is frequently identified and associated with a poor VT-free survival. Patients with a pathogenic mutation often show an anteroseptal scar pattern which, in combination with potential disease progression, may significantly impact ablation outcome.

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Whole human heart histology to evaluate the performance of bipolar and unipolar voltage mapping in the detection of fibrosis in patients with non-ischemic cardiomyopathy and ventricular tachycardia

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Background: Ventricular tachycardias (VTs) in non-ischemic cardiomyopathy (NICM) are related to fibrosis. The identification of fibrosis relies on electroanatomical voltage mapping (EAVM). One cut-off value for Unipolar (UV) (8.27mV) and one for Bipolar Voltage (BV) (1.5mV) are currently used to differentiate between fibrosis and viable myocardium during LV mapping. It has been suggested that BV mapping has limited value for detecting fibrosis in NICM. EAVM has however never been validated by histology in NICM.
Purpose: To establish the performance of BV and UV for the detection of LV fibrosis in NICM.
Methods: Eight patients with NICM and VTs underwent EAVM prior to death or heart transplantation. EAVM data was projected onto images of gross pathological slices of the entire heart through reversed registration. The wall thickness (WT), amount of viable myocardium and proportion of fibrosis was quantified in transmural biopsies corresponding to LV endocardial EAVM sites.
Results: Biopsies (n=277) had a median WT of 14.4mm [IQR 10.7-17.3] with 46.8mm2 viable myocardium [IQR 43.3-59.6] and 25.5% fibrosis [IQR 20.1-33.7]. These biopsies generated UV and BV of 6.2mV [IQR 4.5-9.0] and 2.6mV [IQR 1.6-4.3], respectively. In the absence of abnormal amounts of fibrosis (n=78 biopsies), both UV and BV were significantly affected by myocardial WT (p=0.001 and 0.008). In all biopsies, the amount of viable myocardium throughout the entire transmural biopsy further affected not only UV but also the BV electrogram amplitude (p<0.001 for both UV and BV). Sixty-eight percent of biopsies generating BV>1.5mV and 53% of biopsies generating UV >8.27mV had abnormal amounts of fibrosis indicating that these cut-off values perform poorly at excluding the presence of abnormal fibrosis. As both WT and the amount of viable myocardium showed a linear relationship with both UV and BV, we could generate an equation to predict the amount of fibrosis present at any location, given the ex-vivo WT and UV and/or BV generated (p<0.001 for both UV and BV) (Figure).
Conclusion: UV and BV mapping are sensitive to the WT and the amount of fibrosis. A single UV or BV cut-off value cannot be used to identify fibrosis; however, if WT is known, both UV and BV voltages may be diagnostic for fibrosis in NICM.

A

$$\%\ \text{fibrosis} = \frac{\text{UV} - 4.69 - 0.28(\text{ex vivo wall thickness})}{-0.06}$$

$$\%\ \text{fibrosis} = \frac{\text{BV} - 2.2 - 0.18(\text{ex vivo wall thickness})}{-0.05}$$

B

Fibrosis (%) \ UV	Ex vivo wall thickness (mm) 10	13	16	19
BV 15	6.6 / 3.3	7.5 / 3.8	8.3 / 4.4	9.1 / 4.9
BV 25	6.1 / 2.8	6.9 / 3.4	7.7 / 3.9	8.6 / 4.5
BV 35	5.5 / 2.4	6.4 / 2.9	7.2 / 3.5	8.0 / 4.0
BV 45	5.0 / 1.9	5.8 / 2.5	6.6 / 3.0	7.5 / 3.5

A. Equations to predict amount of fibrosis when wall thickness (mm) and voltages (mV) are known.

B. Voltages (mV) generated when ex-vivo wall thickness (mm) and % fibrosis is known.

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