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Mechanisms contributing to exercise intolerance in patients with atrial fibrillation

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Background: Exercise intolerance is commonly reported in patients with atrial fibrillation (AF) despite preserved ejection fraction. However, the contribution of rhythm, echocardiographic parameters and cardiovascular risk factors to exercise intolerance is poorly understood. Furthermore, recent data shows a high prevalence of heart failure with preserved ejection fraction amongst AF patients, which may contribute to exercise intolerance.
Purpose: Our aim was to evaluate the prevalence of exercise intolerance and its potential contributors amongst a cohort of AF patients undergoing cardiopulmonary exercise testing (CPET).
Methods: We assessed 151 AF patients (34% female) referred for CPET. All patients underwent routine clinical assessment, including detailed evaluation of cardiovascular risk factors, transthoracic echocardiography and a maximal CPET using a modified Balke treadmill protocol. To investigate the contribute of cardiac rhythm to exercise tolerance, CPET was reported in a select cohort of patients with persistent AF, 21 days following electrical cardioversion to sinus rhythm (SR).
Results: The mean age was 67 ± 8 years with a BMI of 29.4 ± 4.4 kg/m^2. 59% of the cohort were in sinus rhythm (SR) at the time of testing. 41% of patients reached a peak VO2 <85% of age and gender predicted values. There was no significant difference in peak VO2 between patients in AF versus SR (p=0.22). After adjustment for age and gender, only chronotropic response (p=0.017) and echocardiographic indices of left ventricular (LV) filling pressures (E/E', p=0.014) were significant predictors of peak VO2. In 20 patients who underwent subsequent cardioversion from AF to SR, peak VO2 improved significantly from 19.7 ± 7.0 to 21.4 ± 6.1 ml/kg/min (p=0.003).
Conclusion: Our main findings are that (i) the main predictors of peak VO2 are chronotropic response to exercise and indices of LV filling pressure, (ii) peak VO2 can be significantly improved in patients with persistent AF by restoration of SR. These findings highlight potential targets alongside rhythm control, for the improvement of exercise tolerance in AF patients.

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Association of non-valvular atrial fibrillation with rs10465885 polymorphism in connexin-40 gene and left ventricular structure and function: propensity score matching analysis

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Purpose: To study the association of non-valvular atrial fibrillation (AF) with rs10465885 polymorphism in connexin-40 (Cx40) gene and left ventricular (LV) structure and function (S-F), including through propensity score matching (PSM) analysis.
Methods: We enrolled 186 patients (pts) under the age of 65 yrs (mean age [M±SD] 55±10) years; males 123 [66,1%]) with non-valvular AF (paroxysmal – 86, persistent – 72, stable – 28 pts). We studied clinical, laboratory and echo data. SNP rs10465885 in Cx40 gene was genotyped by Real-time PCR (T – reference, C – minor allele) in 112 pts. We also enrolled 78 age- and gender-matched healthy controls (60 males [77%]; mean age [51±11] yrs). Genotype distribution of rs10465885 in 1000 Genomes Project pooled European control sample (EUR; n=503) was additionally used as comparator.
Results: Genotype distribution of rs10465885 in controls was as follows: TT – 28,2%; CT – 41,0%; CC – 30,8% (consistent with Hardy-Weinberg principle). The same distribution in AF pts was as follows: TT – 25,9%; CT – 49,1%; CC – 25,0%, – thus being comparable to that in controls (p=0,755). By the use of Artificial Neural Network (ANN) analysis, we identified 5 parameters, associated with rs10465885: age AF onset; heart failure (HF) status; LV posterior wall thickness (PWT); LV mid-wall fractional shortening (MWFS) and LV myocardial mass, indexed by height2.7 (MM/h2.7). According to those parameters, total AF sample was stratified into 2 phenotypic clusters (PC): PC1 (n=67) and PC2 (n=119). PC1, vs. PC2, was characterized by higher frequency of CC variant (37,8% vs. 16,4%, respectively [r]; p=0,010); higher frequency of cases with relatively high "CC" probability, assessed by ANN model (59,1% vs. 13,5%, [r]; p<0,001); and higher total frequency of CC and "CC" (44,8% [95% CI (32,9–56,9%); n=30/67] vs. 15,1% [95% CI (9,2–22,2%); n=18/119], [r]; p<0,001). Total frequency of [CC + "CC"] in PC1 was also higher, than in EUR (25,3% [95% CI 21,5–29,1]; p=0,002). Additionally, PC1, vs. PC2, was characterized by earlier AF onset, predominance of males, higher frequency of "silent" AF cases, absence of HF and less pronounced LV S-F changes. While comparing echo data in PSM-groups (matched by age, sex, frequency of hypertension and its duration), PSM-PC1 (n=30), vs.

PSM-control (n=30), was associated with higher antero-posterior left atrium dimension (LAD) only. At the same time, PSM-PC2 (n=22), vs. corresponding PSM-control (n=22), besides higher LAD, was additionally associated with higher LV PWT, interventricular septum thickness, more compromised LV MWFS, as well as the tendency towards higher MM/h2.7 values.
Conclusion: Non-valvular AF in pts under the age of 65 yrs is associated with rs10465885 in Cx40 gene and LV S-F state, depending on their phenotypic "portrait". The potential genetic AF background should be considered in pts with early AF onset, predominantly males, without HF and overt LV S-F changes, including subclinical AF cases.

ATRIAL FIBRILLATION – ABLATION

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Single procedure outcomes, quality of life, NYHA improvement, and reduced symptoms 12 months post cryoballoon ablation in persistent atrial fibrillation: results from the CRYO4PERSISTENT AF Study

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Background/Introduction: PVI is recognized as the cornerstone of AF ablation, including ablation of persistent AF. To our knowledge, this is the first prospective multicenter study reporting long-term outcomes after a single PVI-only ablation procedure with the cryoballoon in PersAF patients using Arctic Front Advance. Arrhythmia recurrence, quality of life, EHRA AF Symptom Score, NYHA class, and 12-month outcomes were evaluated.
Purpose: The CRYO4PERSISTENT AF study (NCT02213731) is a prospective, multicenter, non-randomized, single arm study to assess single procedure outcomes of pulmonary vein antrum isolation using the cryoballoon.
Methods: The study enrolled patients with persistent AF (diagnosis within 12 months of consent, 100% AF burden of 7–180 days, and/or AF requiring cardioversion) at 11 European sites. The primary endpoint was freedom from AF/AFL/AT recurrence at 12 months, defined as arrhythmias ≥30 seconds or reintervention for AF, excluding a 3-month blanking period. After enrollment, patients without 100% AF burden (18-hour Holter or 3 consecutive ECG recordings in a timeframe ≥14 days) were exited. Patients were followed at 3, 6, and 12 months, with 48-hour Holters at 6 and 12 months. Quality of life, NYHA class, and arrhythmic symptoms were evaluated at 12 months. An independent core lab adjudicated arrhythmia recurrence and adverse events were adjudicated by an independent committee.
Results: A total of 101 patients (62±11 years, 74% male, LVEF 56±8%, LAD 43±5 mm) meeting criteria, undergoing a cryoballoon ablation, with follow-up data, were included in the analysis. At 12 months post-ablation 16% of patients had arrhythmic symptoms compared to 92% at baseline (p<0.0001). Arrhythmia-related symptom reduction was statistically significant 12 months post-ablation for all symptoms except syncope (2% to 0%): dizziness (14% to 2%), palpitations (68% to 8%), rapid heartbeat (27% to 5%), dyspnea (53% to 6%), and fatigue (42% to 4%), all p<0.01. The symptomatic reduction was supported by significant improvement in SF-36v2 scores at 12 months and EHRA AF Symptom Score. The mean normalized SF-36 physical component score improved from 46.9 to 53.9 (p<0.0001) and the mental component score improved from 47.3 to 50.6 (p=0.008). The EHRA AF Symptom Score decreased from 2.1 to 1.3 (p<0.01). NYHA class improvement of ≥1 was observed in 47% of patients at 12 months. Freedom from AF/AFL/AT recurrence was 60.7% at 12 months (1-sided lower 95% confidence bound: 51.1%). The only cryoballoon device related event was transient PNI, observed in 2 patients (2%), with resolution pre-discharge.
Conclusion(s): Persistent AF patients treated with the second generation cryoballoon demonstrated a significant reduction in arrhythmia-related symptoms, improved QOL, a reduced EHRA AF Symptom Score, improvement in NYHA class, and 61% single procedure success rate at 12 months post-ablation. No patients experienced PNI post-discharge.

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Mechanical inducibility of atrial fibrillation in pulmonary vein isolation procedures is associated with inferior outcome: a propensity score matched analysis

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Introduction: In pulmonary vein isolation (PVI) procedures, a mechanical induction of atrial fibrillation may be observed. However, data about the impact of mechanical inducibility on outcome after PVI is scarce.