mice showed a significant reduction in the cardiomyocyte cross sectional area (sham, $267 \pm 3.4 \mu\text{m}^2$, vehicle treated TAC mice, $480 \pm 5.8 \mu\text{m}^2$, AP2 treated TAC mice, $319 \pm 3.9 \mu\text{m}^2$). A significant reduction in the expression of the hypertrophic marker ANP and BNP and in the percentage of fibrosis was also observed in these mice compared with vehicle treated TAC mice. AP2 treatment led to a significant reduction in the expression of the bona fide calcineurin target RCAN1.4 and a reduction in the NFAT phosphorylation level in vivo and the NFAT transcriptional activity in vitro. In conclusion, we have identified AP2 as a novel PMCA4 specific inhibitor and shown its potential to modify the development of cardiac hypertrophy likely through inhibition of calcineurin/NFAT signalling. This compound has drug-like properties and thus lays the basis for a novel approach for treating cardiac hypertrophy and failure through PMCA4 inhibition.

145 CHARACTERISATION OF FRACTIONATED ATRIAL ELECTROGRAMS CRITICAL FOR MAINTENANCE OF AF: A RANDOMISED CONTROLLED TRIAL OF ABLATION STRATEGIES (THE CFAE AF TRIAL)

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Introduction Targeting complex fractionated atrial electrograms (CFAE) in the ablation of atrial fibrillation (AF) may improve outcomes, although whether this is by eliminating focal drivers or simply de-bulking atrial tissue is unclear. It is also uncertain what electrogram morphology should be ablated. This randomised study aimed to determine the impact of ablating different CFAE morphologies compared to normal electrograms (ie, de-bulking normal tissue) on the cycle length of persistent AF (AFCL).

Methods After pulmonary vein isolation CFAE were targeted systematically throughout the left then right atrium, until termination of AF or abolition of CFAE prior to DC cardioversion. 10 s electrograms were classified by visual inspection according to a validated scale, with Grade 1 being most fractionated and grade 5 normal. Patients were randomised to have CFAE grades eliminated sequentially, from grade 1 to 5 (group 1) or grade 5 to 1 (group 2). Because grade 5 electrograms were considered normal, only 5 were ablated. Mean AFCL was determined manually over 30 cycles from bipolar electrograms recorded at the left and right atrial appendages before and after each CFAE was targeted. Lesions were regarded as individual observations, and a resultant increase in mean AFCL ≥ 5 ms was regarded as significant. The randomised strategy first controlled for any cumulative effect of ablation on AFCL, and second allowed assessment of the order of ablation on the number of CFAE lesions required.

Results 20 patients were randomised. The CFAE grade determined by rapid visual inspection for the 968 electrograms targeted agreed with that at off-line manual measurement in 92.7% ($\kappa=0.91$). AFCL increased after targeting 49.5% of grade 1 CFAE, 33.6% of grade 2, 12.8% of grade 3, 33.0% of grade 4, and 8.2% of grade 5 CFAE ($p<0.0001$ for grades 1, 2, and 4 vs 5, 3 vs 5 not significant). Binary logistic regression confirmed the effect of CFAE grade, but showed no effect of electrogram amplitude, location in the left or right atrium, or the order in which CFAE were targeted. There was no difference between groups in the number of grade 1 or 2 CFAE encountered, but there were fewer grade 3 and 4 CFAE in group 2 than group 1 (both $p<0.01$), translating to fewer CFAE targeted per patient in group 1 compared to group 2 (37 ± 14 and 58 ± 18 respectively; $p=0.015$).

Conclusion Targeting CFAE is not simply atrial de-bulking. Ablating certain grades of CFAE caused AFCL prolongation, suggesting they are more important in maintaining AF. Targeting these CFAE may reduce unnecessary left atrial destruction. (ClinicalTrials.gov number, NCT00894400).

Abstract 145 Figure 1 Impact of CFAE grade on the proportion of lesions causing AF cycle length prolongation.

146 IS THERE AN ASSOCIATION BETWEEN THROMBOGENESIS MARKERS AND ATRIAL FIBRILLATION BURDEN IN PACEMAKER POPULATION?

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Background and Objectives Contemporary pacemaker devices are able to quantify atrial high-rate episodes (AHREs) and atrial fibrillation burden (AFB) accurately. In this study, we aim to assess the relationship of thrombogenesis markers in association with AHREs and AFB.

Methods We studied 87 patients with dual-chamber pacemaker. Patients on warfarin were excluded. AHREs were defined as atrial rate ≥ 220 beats/min and ≥ 5 minutes. AFB and percentage of cumulative pacing were derived from pacemaker diagnostics. Plasma levels of von Willebrand factor (vWf), tissue factor (TF), soluble P-selectin (P-sel) and D-dimer (DDM) were analysed using ELISA.

Results Baseline characteristics and co-morbidities were comparable between groups (Abstract 146 table 1). Patients with AHREs had significantly higher cumulative percentage ventricular pacing ($p=0.012$). There were no significant differences in levels of vWf, TF, P-sel and DDM between patients with and without AHREs. The AFB ranged from 0 to 99% in AHRE group. TF ($r=0.516$, $p=0.086$), P-sel ($r=0.795$, $p<0.001$) and DDM ($r=0.643$, $p=0.045$) correlated with AFB. On linear regression analysis, both P-sel and DDM were independently associated with AFB ($p<0.05$).

Abstract 146 Table 1

	No AHRE (n = 70)	AHRE (n = 17)	p value
Age, years	71.0 $\pm$ 11.6	75.4 $\pm$ 8.8	0.096
Hypertension, (%)	38, (54)	12, (71)	0.116
Antiplatelet, (%)	53, (76)	14, (82)	0.739
Percentage atrial pacing	34.6 (6.8–81.5)	22.1 (6.9–65.0)	0.414
Percentage ventricular pacing	21.9 (1.8–99.0)	98.6 (41.0–99.9)	0.012
vWf, IU/dl	94.2 $\pm$ 16.2	93.9 $\pm$ 33.7	0.977
TF, ng/ml	0.2 (0.1–0.3)	0.1 (0.0–0.2)	0.105
P-sel, ng/ml	47.6 $\pm$ 15.8	63.4 $\pm$ 29.7	0.055
DDM, ng/ml	180.0 (82.0–390.0)	152.5 (82.5–307.5)	0.553