SUPPLEMENTAL MATERIAL

Supplemental Table 1. Ambulatory ECG Holter data of sham and bigeminal PACs and PVCs.

	Sham (n=9)	**PAC (n=7)**	**PVC (n=11)**	**P-value**
Mean HR (bpm)	99.0±1.4	119.1±3.2*	122.5±4.4*	<0.001
PACs no. (%)	4770±1447 (3.5)	64865±8015 (40.1)*	106±37 (0.5)†	<0.001
PVCs no. (%)	745±257 (1)	1.1±1 (0.4)	86499±11636 (49.8)*†	<0.001

Footnote: Values are mean ± SEM. % indicates the percentage of PACs or PVCs ("burden") of the total beat count during 24-hr Holter monitoring. Multiple comparison test: * and † indicate $p<0.05$ vs. sham and PAC groups, respectively. HR: Heart rate; PAC: premature atrial contraction; PVC: premature ventricular contraction.

Supplemental Table 2. Echocardiographic parameters of sham, PAC and PVC groups during the 12-week protocol.

	Sham (n=9)	PAC (n=7)	PVC (n=11)	p-value
LVEF (%)				**<0.0001**
Baseline	60.0 ± 1.1	62.9 ± 1.7	61.4 ± 0.5	
Week-4	57.7 ± 0.9	59.9 ± 1.8	50.2 ± 1.5 *†‡	
Week-8	58.4 ± 1.3	56.6 ± 1.8	44.9 ± 1.9 *†‡	
Week-12	58.8 ± 0.9	56.1 ± 1.9 ‡	44.2 ± 1.7 *†‡§	
LVEDV (mL)				**<0.0001**
Baseline	50.9 ± 2.4	50.4 ± 1.6	50.6 ± 1.2	
Week-4	49.4 ± 2.4	53.6 ± 2.0	56.1 ± 1.8 ‡	
Week-8	51.1 ± 2.8	48.7 ± 1.9	61.9 ± 3.0 *†‡	
Week-12	51.7 ± 2.1	51.3 ± 1.7	64.5 ± 2.1 *†‡§	
LVESV (mL)				**<0.0001**
Baseline	20.6 ± 1.2	18.4 ± 0.7	19.5 ± 0.5	
Week-4	21.2 ± 0.9	21.6 ± 0.6 ‡	28.1 ± 1.6 *†‡	
Week-8	21.1 ± 1.6	21.1 ± 1.1	32.5 ± 2.4 *†‡	
Week-12	21.3 ± 0.8	22.4 ± 1.5 ‡	35.9 ± 1.9 *†‡§	
IVSEDD (cm)				0.699
Baseline	0.90 ± 0.02	0.89 ± 0.05	0.91 ± 0.02	
Week-4	0.91 ± 0.03	0.86 ± 0.03	0.89 ± 0.03	
Week-8	0.89 ± 0.04	0.89 ± 0.05	0.96 ± 0.03	
Week-12	0.92 ± 0.04	0.93 ± 0.04	0.98 ± 0.03	
PWEDD (cm)				0.990
Baseline	0.89 ± 0.03	0.84 ± 0.05	0.85 ± 0.03	
Week-4	0.88 ± 0.01	0.83 ± 0.03	0.87 ± 0.04	
Week-8	0.91 ± 0.04	0.84 ± 0.05	0.86 ± 0.04	

Week-12	0.87 ± 0.02	0.83 ± 0.03	0.85 ± 0.05	
LVEDD (cm)				**<0.010**
Baseline	3.91 ± 0.12	3.83 ± 0.12	3.87 ± 0.10	
Week-4	3.98 ± 0.12	3.99 ± 0.15	4.30 ± 0.14 ‡	
Week-8	3.99 ± 0.11	3.87 ± 0.15	4.36 ± 0.17	
Week-12	3.90 ± 0.08	3.81 ± 0.15	4.55 ± 0.13 *†‡	
LVESD (cm)				**<0.001**
Baseline	2.40 ± 0.12	2.40 ± 0.12	2.55 ± 0.07	
Week-4	2.52 ± 0.11	2.70 ± 0.11 ‡	3.08 ± 0.13 *‡	
Week-8	2.48 ± 0.08	2.63 ± 0.13	3.17 ± 0.14 *†‡	
Week-12	2.54 ± 0.09	2.61 ± 0.09	3.37 ± 0.11 *†‡	
E/A ratio				0.661
Baseline	1.7 ± 0.1	1.8 ± 0.2	1.7 ± 0.1	
Week-4	1.7 ± 0.1	1.8 ± 0.1	1.4 ± 0.1	
Week-8	1.7 ± 0.1	1.8 ± 0.1	1.4 ± 0.2 †	
Week-12	1.6 ± 0.1	1.9 ± 0.2	1.4 ± 0.1 †	

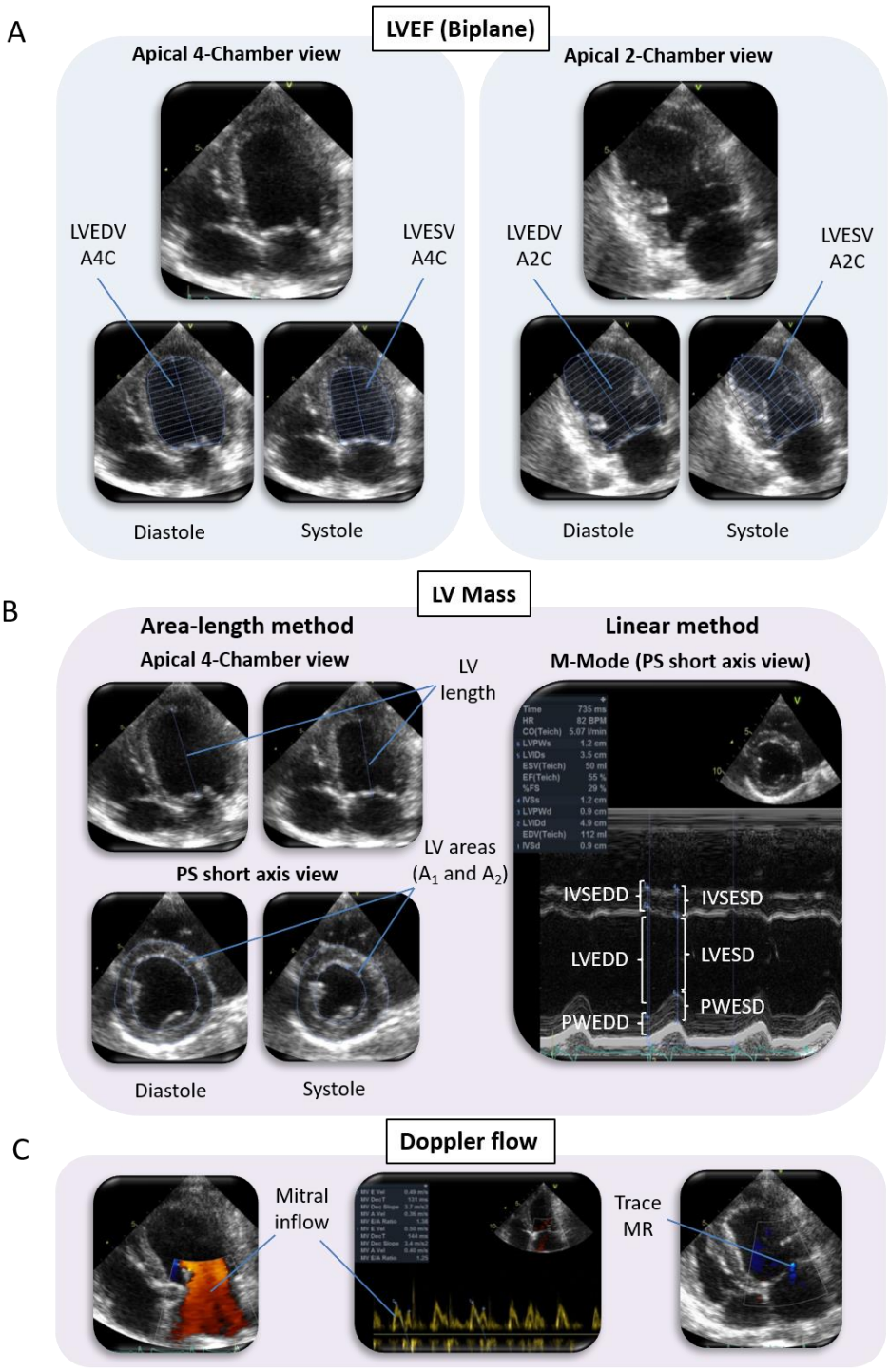
Footnote: Values are mean ± SEM. Multiple comparison test ($p<0.05$): * vs sham, † vs PAC, ‡ vs baseline and § vs week-4. PAC: premature atrial contraction; PVC: premature ventricular contraction; LVEF: left ventricular ejection fraction; LVEDV: left ventricular end-diastolic volume; LVESV: left ventricular end-systolic volume; IVSEDD: interventricular end-diastolic dimension; PWEDD: posterior wall end-diastolic dimension; LVEDD: left ventricular end-diastolic dimension; LVESD: left ventricular end-systolic dimension; E/A: mitral ratio of peak early to late diastolic filling velocity.

Supplemental Table 3. Left ventricular RWT and mass index (estimated by 2 methods) of sham, PAC and PVC groups during the 12-week protocol.

	Sham (n=9)	**PAC (n=7)**	**PVC (n=11)**	**p-value**
LV Mass index (Linear method, g/kg)				**<0.001**
Baseline	4.8 ± 0.3	4.6 ± 0.3	4.6 ± 0.3	
Week-4	4.9 ± 0.2	4.7 ± 0.3	5.5 ± 0.5 ‡	
Week-8	5.0 ± 0.3	4.7 ± 0.3	5.9 ± 0.5 ‡	
Week-12	4.8 ± 0.2	4.7 ± 0.3	6.3 ± 0.5 *†‡§	
LV Mass index (Area-length, g/kg)				**<0.0001**
Baseline	3.7 ± 0.1	3.5 ± 0.1	3.6 ± 0.2	
Week-4	3.7 ± 0.1	3.6 ± 0.1	4.0 ± 0.2 ‡	
Week-8	3.7 ± 0.2	3.7 ± 0.2	4.3 ± 0.2 ‡§	
Week-12	3.8 ± 0.1	3.8 ± 0.1	4.5 ± 0.2 *†‡§	
RWT				0.642
Baseline	0.46 ± 0.02	0.44 ± 0.03	0.44 ± 0.02	
Week-4	0.45 ± 0.02	0.42 ± 0.03	0.41 ± 0.01	
Week-8	0.46 ± 0.02	0.44 ± 0.04	0.40 ± 0.02	
Week-12	0.45 ± 0.01	0.44 ± 0.03	0.37 ± 0.02 *‡	

Footnote: Values are mean ± SEM. Multiple comparison test ($p<0.05$): * vs sham, † vs PAC, ‡ vs baseline and § vs week-4. PAC: premature atrial contraction; PVC: premature ventricular contraction; LV: left ventricle; RWT: relative wall thickness.

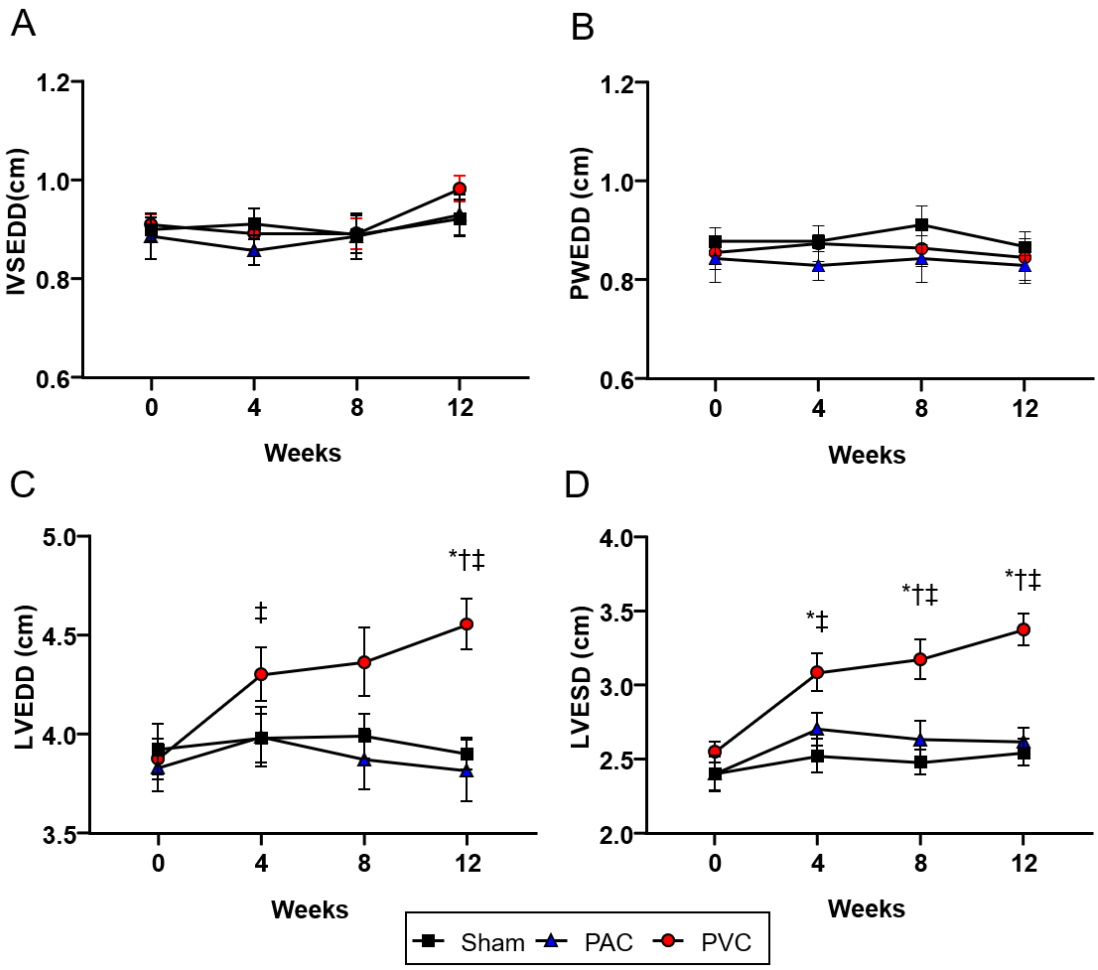
Supplemental Figure 1. Echocardiographic views, methods and parameters to assess left ventricular function and structure.



Footnote: (**A**). LVEF was quantified using the biplane method of disks (modified Simpson's rule), based on the acquisition of images of the LV from the apical 4- and 2-chamber views. (**B**). LV mass was estimated by two methods: (Right) Linear method, based in the Cube formula and LV linear dimensions

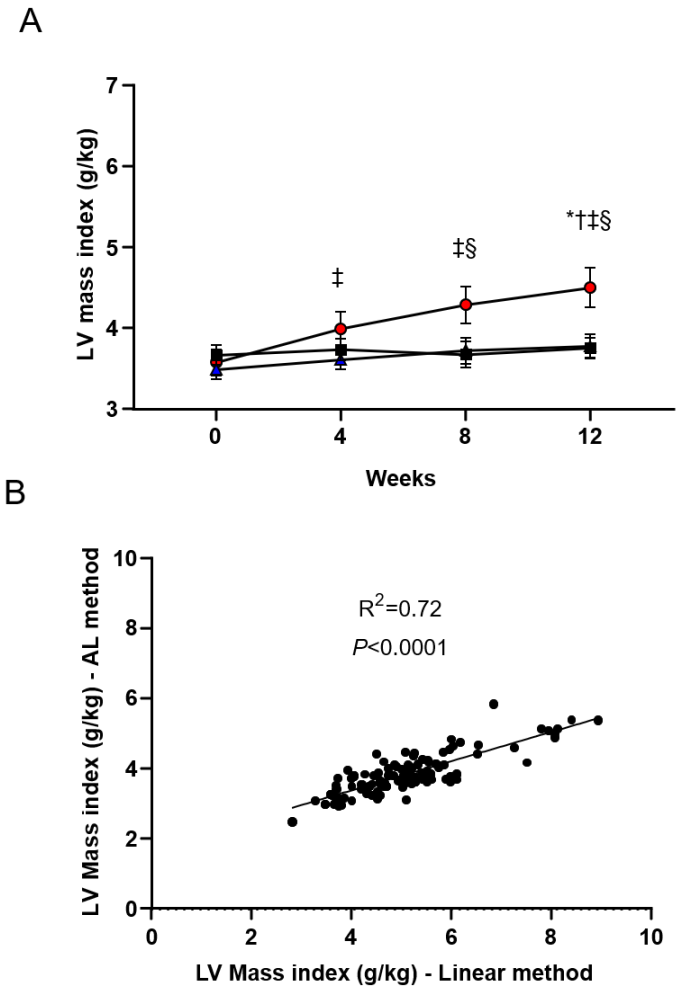
derived with a two-dimensional echocardiography-guided M-mode approach in the PS short-axis view at the level of the papillary muscles; (Left) Area-length method, which is based in the Area-length formula and the assessment of epicardial (A_1) and endocardial (A_2) cross-sectional areas obtained in the PS short-axis view (with the papillary muscles considered part of the LV cavity). LV cavity length is measured in 4 apical-chamber view as the distance from apex to the mid mitral annulus plane (see text for more details). LV cross-sectional areas and lengths were obtained at systole and diastole and averaged. (**C**). Doppler-ultrasound techniques (i.e., pulsed-wave and color flow imaging) were performed to measure the mitral inflow velocities and to evaluate for MR. LVEF: left ventricular ejection fraction; LVEDV: left ventricular end-diastolic volume; LVESV: left ventricular end-systolic volume; A4C and A2C: apical 4- and 2-chamber view, respectively; LV: left ventricle; PS: parasternal; IVSEDD: interventricular septal end-diastolic dimension; LVEDD: left ventricular end-diastolic dimension; PWEDD: posterior wall end-diastolic dimension; IVSESD: interventricular septal end-systolic dimension; LVESD: left ventricular end-systolic dimension; PWESD: posterior wall end-systolic dimension; MR: mitral regurgitation.

Supplemental Figure 2. Changes in LV linear dimensions assessed by M-mode echocardiography in the study groups over the 12-week protocol.



Footnote: LV: left ventricle; PVC: premature ventricular contraction; PAC: premature atrial contraction; IVSEDD: interventricular septal end-diastolic dimension; PWEDD: posterior wall end-diastolic dimension; LVEDD: left ventricular end-diastolic dimension; LVESD: left ventricular end-systolic dimension.

Supplemental Figure 3. Changes in LV mass index in the study groups during the 12-week protocol assessed by the Area-length method and its correlation with the Linear method.



Footnote: (**A**). The progressive increase in LV mass index induced by PVC bigeminy during the 12-week protocol (Figure 4A) was corroborated by the Area-length method, whose values are independently derived to those obtained by the Linear method. (**B**). Correlation between the two echocardiographic methods by plotting all values of the study groups at all time points. These two methods showed a positive and significant correlation (R^2=0.72; *P*<0.0001). Note that absolute values of LV mass index gathered by the Linear method were higher than those estimations obtained by the area-length method. For more detailed information see the text. LV: left ventricule; AL: area-length.