SUPPLEMENTARY MATERIAL

Supplemental Appendix S1. Supplemental Methods

Echocardiographic measurements

The assessment included atrial and ventricular chamber wall thickness, dimensions, area and calculated volumes. Left atrial volume was calculated with the area-length method from 2- and 4-chamber views according to guidelines. Left ventricular wall thickness was assessed from the parasternal short axis view and LV-mass calculated (Deveraux et al 1986). Right ventricular free wall thickness was measured from the apical 4-chamber view (Cooper et al 1984). Respiratory variations in inferior cava diameter and left ventricular eccentricity index (both with B-mode), hepatic vein, pulmonary vein, bilateral ventricular inflow and outflows were recorded with PWD during instructed light nasal breathing with mouth closed. Left ventricular fractional shortening, ejection fraction, MAPSE as well as right ventricular fractional area change, TAPSE were assessed. Valvular regurgitations were documented when present, and right sided pressures estimated from tricuspid and pulmonary valve regurgitation Doppler traces. In addition, the mitral valve inflow propagation velocity was assessed with colour M-mode. PWD-TDI recordings from mitral valve lateral, septal and tricuspid valve were obtained from the apical 4 chamber view. Left ventricular longitudinal and basal circumferential as well as right ventricular free wall peak systolic strain and strain rates were assessed from apical and parasternal views with speckle tracking. The appearance of the pericardium (thickening, echolucency and/or effusion) was documented subjectively with B-mode from standard apical and parasternal views.

Cooper MJ, Teitel DF, Silverman NH, Enderlein M. Comparison of M-mode echocardiographic measurement of right ventricular wall thickness obtained by the subcostal and parasternal approach in children. Am J Cardiol. 1984 Oct 1;54(7):835-8.

Devereux RB, Alonso DR, Lutas EM, Gottlieb GJ, Campo E, Sachs I et al. Echocardiographic assessment of left ventricular hypertrophy: Comparison to necropsy findings. Am J Cardiol 1986; 57: 450–458.

Supplemental Table S1. Clinical history, medications and procedures in MUL patients

	MUL (N=23)	
Pericardiectomy	5+1	Age at procedure 10m, 3y, 5y, 5y, 6y, and 8y. Clearly thickened pericardium in 3, partly thickened in 1, and thin and adherent in 2 patients.
Secundum atrial septal defect	2	1. Percutaneous device closure 2y 2. No intervention
Wolf-Parkinson-White	2	1. RF-ablation 13y 2. No intervention
Prematurity	2	1. Born gw 30, birthweight 650g, RDS/BPD diagnoses, long-term intermittent CPAP. 2. Born gw 31, severe growth restriction and failure to thrive, RDS/BPD diagnoses, WPW/SVT, no long-term respiratory support.
Diagnostic caths	6	Mean 12-20 mmHg bilateral end-diastolic pressures, no difference between right and left end-diastolic pressures or signs of pulmonary hypertension (>25 mmHg).
Diuretic medication	3	Furosemide and spironolactone
B-blocker medication	2	Bisoprolol

Data is presented as count (N).

Supplemental Table S2. Cardiac atrial and ventricular dimensions among MUL patients and healthy controls

	MUL (N=23)		**Controls (N=23)**		**Adj for BSA**		
	Mean	**SD**	**Mean**	**SD**	**Mean difference**	**CI**	**95%**
Right atrium							
Major axis (cm)	3.30	0.65	3.77	0.64	0.095	-0.145	0.335
Minor axis (cm)	3.07	0.53	3.35	0.56	0.149	-0.099	0.397
Area (cm2)	8.55	2.85	10.96	3.53	0.488	-0.596	1.572
Area indexed (cm2/m2)	11.67	3.34	9.67	1.06	0.768	-0.575	2.523
Right ventricle							
Short axis dimension (cm)	1.44	0.42	1.89	0.54	-0.084	-0.310	0.143
Length (cm)	4.24	0.71	5.55	0.96	-0.564***	-0.876	-0.261
Base (cm)	2.38	0.40	2.58	0.41	0.099	-0.101	0.299
Mid-cavitary diameter (cm)	1.83	0.32	2.25	0.55	-0.093	-0.313	0.128
Anterior wall thickness (cm)	0.39	0.07	0.42	0.09	0.028	-0.015	0.070
Area (cm2)	7.14	1.92	11.13	3.84	-0.142*	-2.616	-0.223
Left atrium							
Antero-posterior length (cm)	2.60	0.43	2.68	0.45	0.275**	0.086	0.464
AP-length/Aortic valve - ratio	2.08	0.27	1.71	0.24	0.276***	0.116	0.437
Major axis (cm)	3.49	0.57	3.77	0.60	0.208	-0.040	0.455
Area (cm2)	8.00	2.56	10.56	3.03	-0.150	-1.217	0.916
Volume (ml)	16.5	8.83	24.33	10.63	0.870	-2.576	4.316
Volume indexed (ml/m2)	21.22	6.28	20.87	3.92	0.856	-2.697	4.408
Left ventricle							
Short axis diameter (cm)	3.65	0.58	4.06	0.63	0.131	-0.039	0.301
Septal thickness (cm)	0.53	0.10	0.64	0.13	-0.014	-0.066	0.038
Posterior wall thickness (cm)	0.60	0.13	0.63	0.11	0.059*	0.001	0.118
Length (cm)	4.7	0.9	6.5	1.0	-0.842***	-1.128	-0.556
Base (cm)	2.4	0.5	2.7	0.4	0.157	-0.021	0.334
Area (cm2)	11.7	3.9	19.0	5.3	-2.85***	-4.10	-1.60
Mass (g)	55.9	24.1	78.8	3.,6	6.25	-1.66	14.2
Mass indexed (g/m2.7)	42.6*	14.4	33.6	8.3	1.84	-4.61	8.29
Mass Z-score for height	-0.69	1.33	-1.06	0.89	0.280	-0.488	1.048

Data is presented as mean (SD). *p<0.05, **p<0.01, and ***p<0.001.

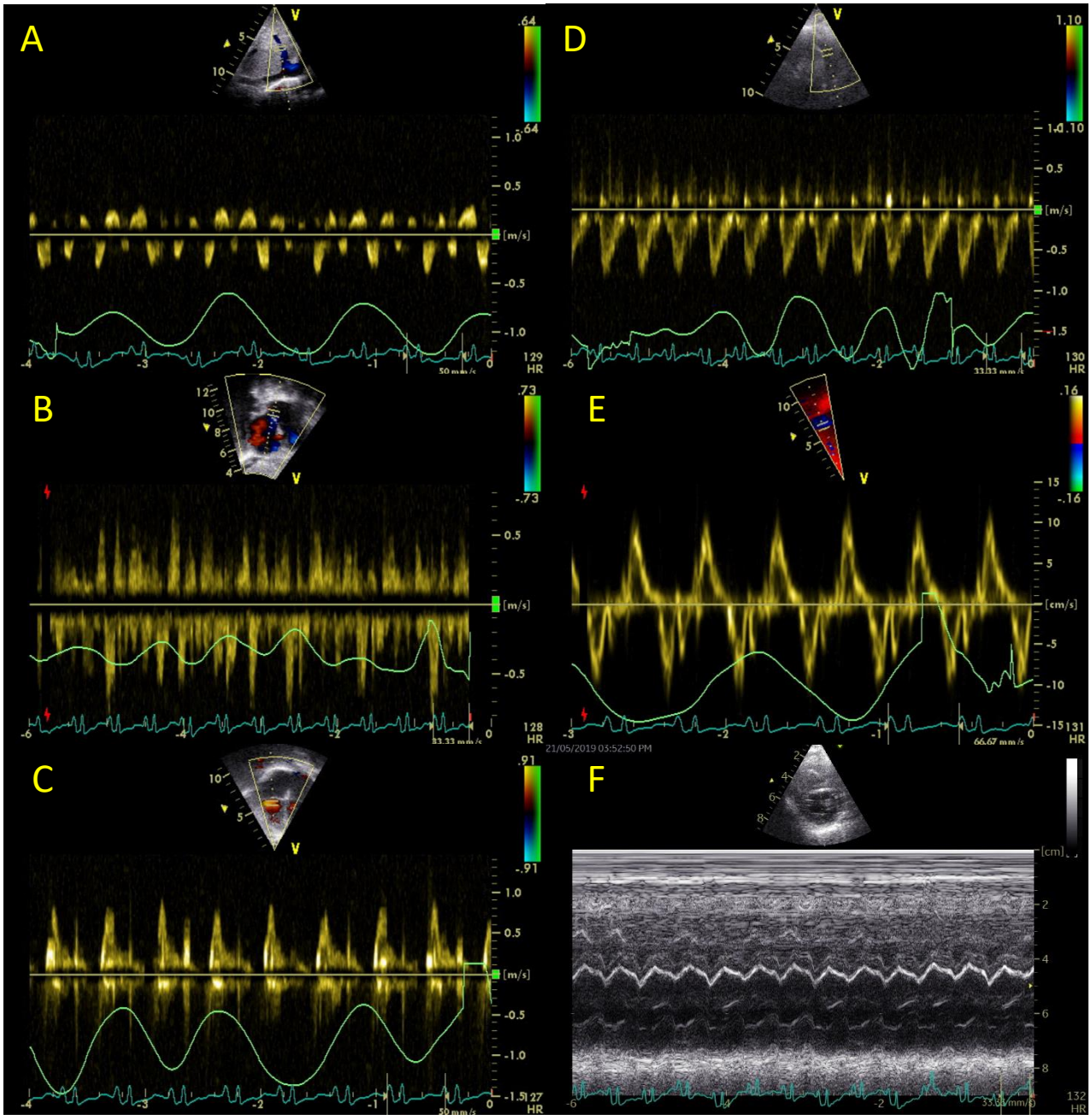
Supplemental Table S3. Cardiac inflows and outflows, and measures of systolic and diastolic function at end-expiration

	MUL (N=23)		**Controls (N=23)**		
	Mean	**SD**	**Mean**	**SD**	**P-value**
Right heart					
Hepatic vein					
S-wave velocity (cm/s)	34	10	31	7	0.442
D-wave velocity (cm/s)	29	11	21	5	0.005
S/D -ratio	1.26	0.48	1.54	0.46	0.049
A-wave velocity (cm/s	24	9	18	4	0.014
A-wave duration (ms)	128	42	83	29	0.001
Tricuspid inflow					
E-wave velocity (cm/s)	47	9	51	11	0.130
A-wave velocity (cm/s)	34	12	26	8	0.018
A-wave duration (ms)	106	22	101	20	0.467
E:A -ratio	1.5	0.5	2.1	0.6	0.002
Pulsed wave tissue Doppler					
TV E' (cm/s)	12.5	5.1	14.6	2.6	0.088
TV A' (cm/s)	7.6	3.1	7.8	1.9	0.785
TV S' (cm)	9.7	3.0	12.0	1.3	0.002
TAPSE (cm)	1.37	0.36	1.96	0.28	0.001
TAPSE/L (no unit)	0.33	0.09	0.36	0.06	0.172
RV-FAC (%)	44	7	42	7	0.415
Ventricular strain imaging					
RVFWGLS (%)	-21.9	5.7	-27.0	6.0	0.007
Left heart					
Pulmonary vein					
PV S-wave velocity (cm/s)	49	10	43	11	0.050
PV D-wave velocity (cm/s)	69	15	55	11	0.001
PV S/D -ratio	0.74	0.21	0.79	0.24	0.465
Mitral inflow					
E-wave velocity (cm/s)	102	22	91	18	0.047
A-wave velocity (cm/s)	45	13	34	13	0.004
A-wave duration (ms)	113	26	96	21	0.022
E/A -ratio	2.33	0.47	2.95	1.05	0.013
Mitral early propagation velocity (cm/s)	54	20	68	16	0.025
Pulsed wave tissue Doppler					
MV E' (cm/s)	17.1	3.0	18.7	3.9	0.147
MV A' (cm/s)	4.8	1.5	6.6	1.4	0.001
MV E:E' -ratio	6.38	1.57	5.20	2.05	0.042
MV S' (cm/s)	7.2	1.3	8.1	1.5	0.039
Septal E'(cm/s)	12.3	2.5	13.1	1.4	0.160
Septal A' (cm/s)	5.6	1.2	5.2	1.0	0.293
Septal E:E' -ratio	8.85	2.67	6.94	1.47	0.005
Septal S' (cm/s)	6.5	1.4	7.5	0.7	0.005
MAPSE (cm)	1.00	0.22	1.40	0.21	0.001
MAPSE/L (no unit)	0.22	0.05	0.22	0.02	0.915

LV-FS (%)	29	6	30	4	0.519
LV-EF (Simpson BP, %)	56	7	56	6	0.724
Ventricular strain imaging					
LV-4GLS (%)	-18.9	4.3	-20.2	2.7	0.237
LV-2GLS (%)	-22.9	5.0	-22.8	2.5	0.447
LV-GBCS (%)	-20.2	3.2	-19.7	2.7	0.525

Data is presented as mean (SD) or as count and percentage. GBCS, Global basal circumferential strain; GLS, Global longitudinal strain; RVFWGLS, Right ventricle free wall global longitudinal strain. TAPSE, tricuspid annular plane systolic excursion; TAPSE/L, TAPSE divided by ventricular length; MAPSE, mitral annular plane systolic excursion, MAPSE/L, MAPSE divided by ventricular length. FS, fractional shortening; EF, ejection fraction.

Supplemental Figure S1. Sample images of respiratory changes in hepatic vein flow (A), right ventricular inflow (C) and outflow (D), inter-atrial right to left shunting on inspiration (B), right ventricular free wall longitudinal PWD TDI tracing (E), and septal curvature (M-mode, F) in a 3 year MUL patient prior to pericardiectomy. Note absence of respiratory changes in hepatic and right ventricular inflows and septal bouncing during respiration due to interatrial shunting in secundum atrial septal defect. Right ventricular free wall PWD TDI tracing is normal.



Supplemental Figure S2. Plasma pro-BNP levels in MUL patients with (MUL PC+, closed circles) and without (MUL PC-, open circles) history of pericardiectomy displayed for age.