

Supplemental material

Supplementary Table 1: General Characteristics of the ATTRv patients.

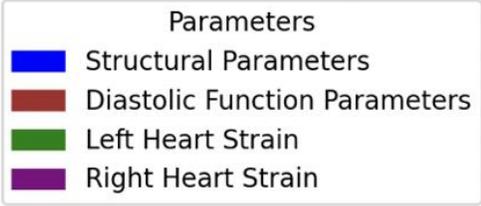
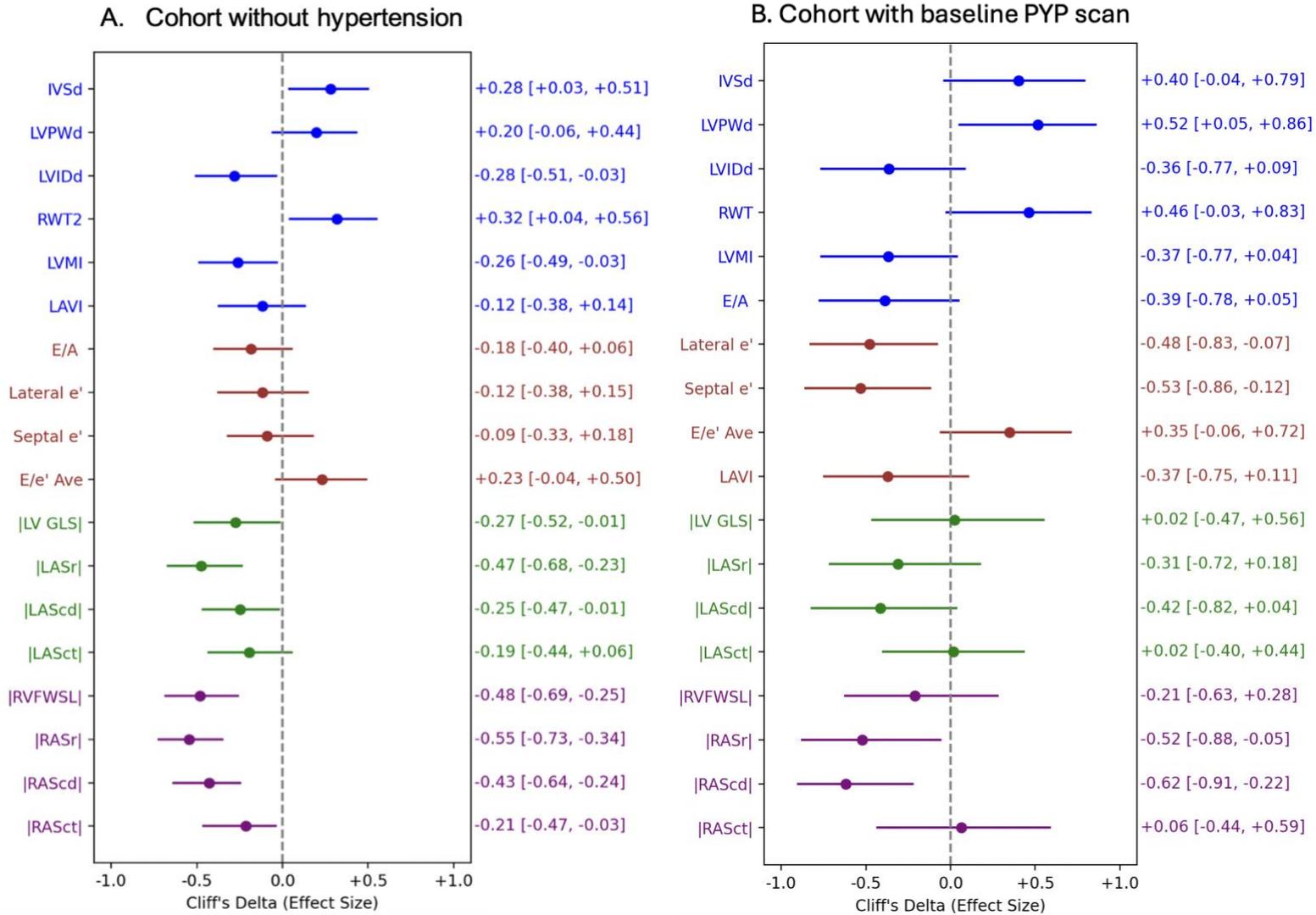
		TTR variant Carriers n=38	ATTRv-CM patients n=43
Age, y ^a		51±11	68±10
Females, n (%)		27 (71%)	9 (21%)
Body mass index, kg/m ²		26.6 [23.6-33.2]	25 [22-27]
Systolic BP, mm Hg		122 [112-137]	120 [115-132]
Diastolic BP, mm Hg		76 [69-82]	74 [63-79]
Race, n (%)	White	27 (71%)	21 (49%)
	Black	7 (19%)	16 (37%)
	Asian	2 (5%)	4 (9%)
	Not reported	2 (5%)	2 (5%)
Comorbidities, n (%)	Hypertension	7 (18%)	22 (51%)
	Atrial fibrillation	-	7 (16%)
	Diabetes mellitus	-	6 (14%)
	CKD	-	6 (14%)
NYHA	Class I	38 (100%)	12 (28%)
	Class II	-	22 (51%)
	Class III	-	9 (21%)
	Class IV	-	-
NTproBNP, pg/ml ^b		53 [28-77]	812 [31- 1630]
Creatinine, mg/dL		0.87 [0.76-0.97]	1.07 [0.95- 1.3]
eGFR, ml/min/1.73m ²		84.0 [74.0- 97.0]	68.5 [56.0 85.0]
TTR gene variants, n (%)	V30M	11 (29%)	9 (21%)
	V122I	9 (24%)	16 (37%)
	T60A	10 (26%)	7 (16%)
	Others	8 (21%)	11 (26%)

^a Age is reported in mean ±SD, the rest as median [IQR 25th-75th].

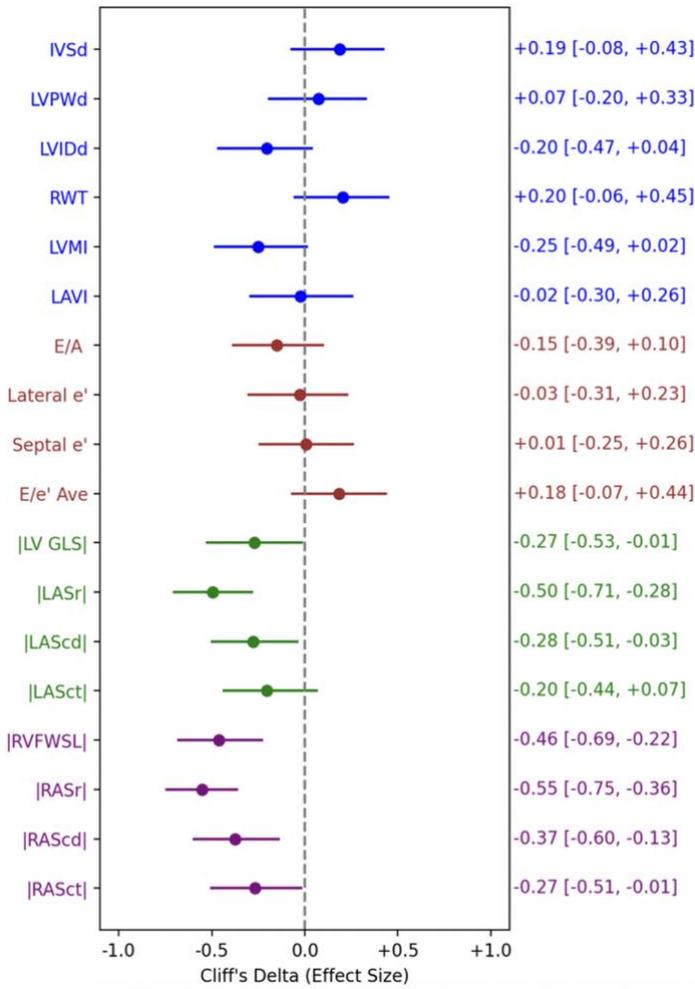
^b NTproBNP values were available for n=31 in the TTR variant carriers group and n=39 in the ATTRv-CM group.

Supplemental Figure 1: Sensitivity analyses of effect sizes: TTR variant Carriers VS matched controls.

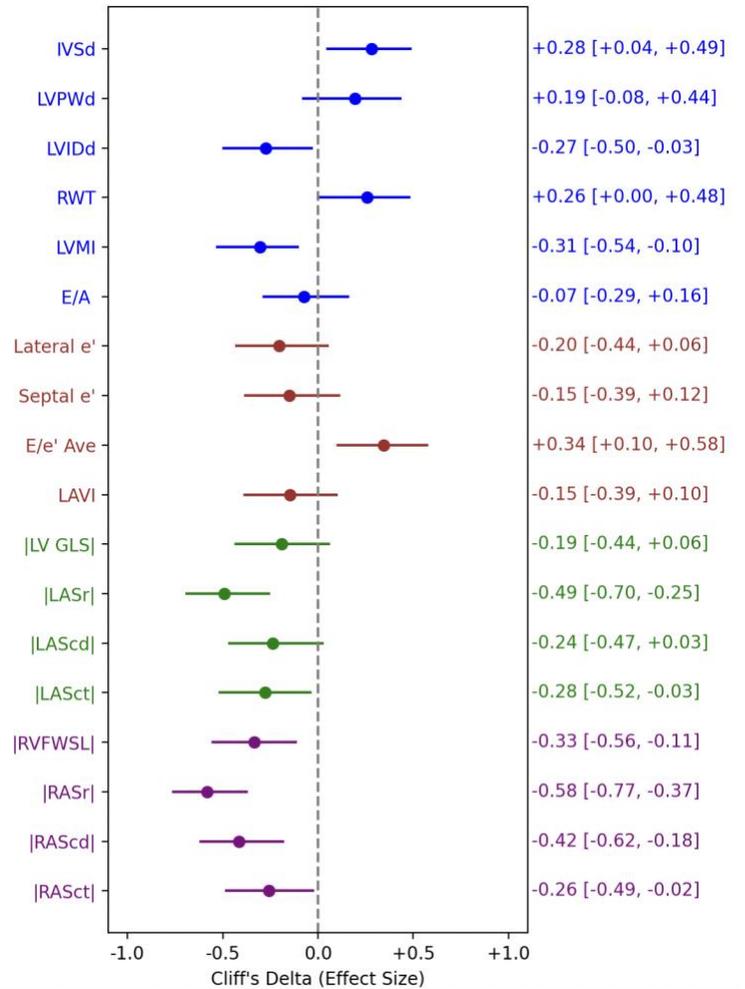
- (A) TTR variant carriers without hypertension (n=30) vs. matched controls (n=60).
- (B) TTR variant carriers with baseline PYP scan (n=10) vs. matched controls (n=20).
- (C) TTR variant carriers without baseline PYP scan (n=28) vs. matched controls (n=54).
- (D) TTR variant carriers >40 years old (n=32) vs. matched controls (n=64).



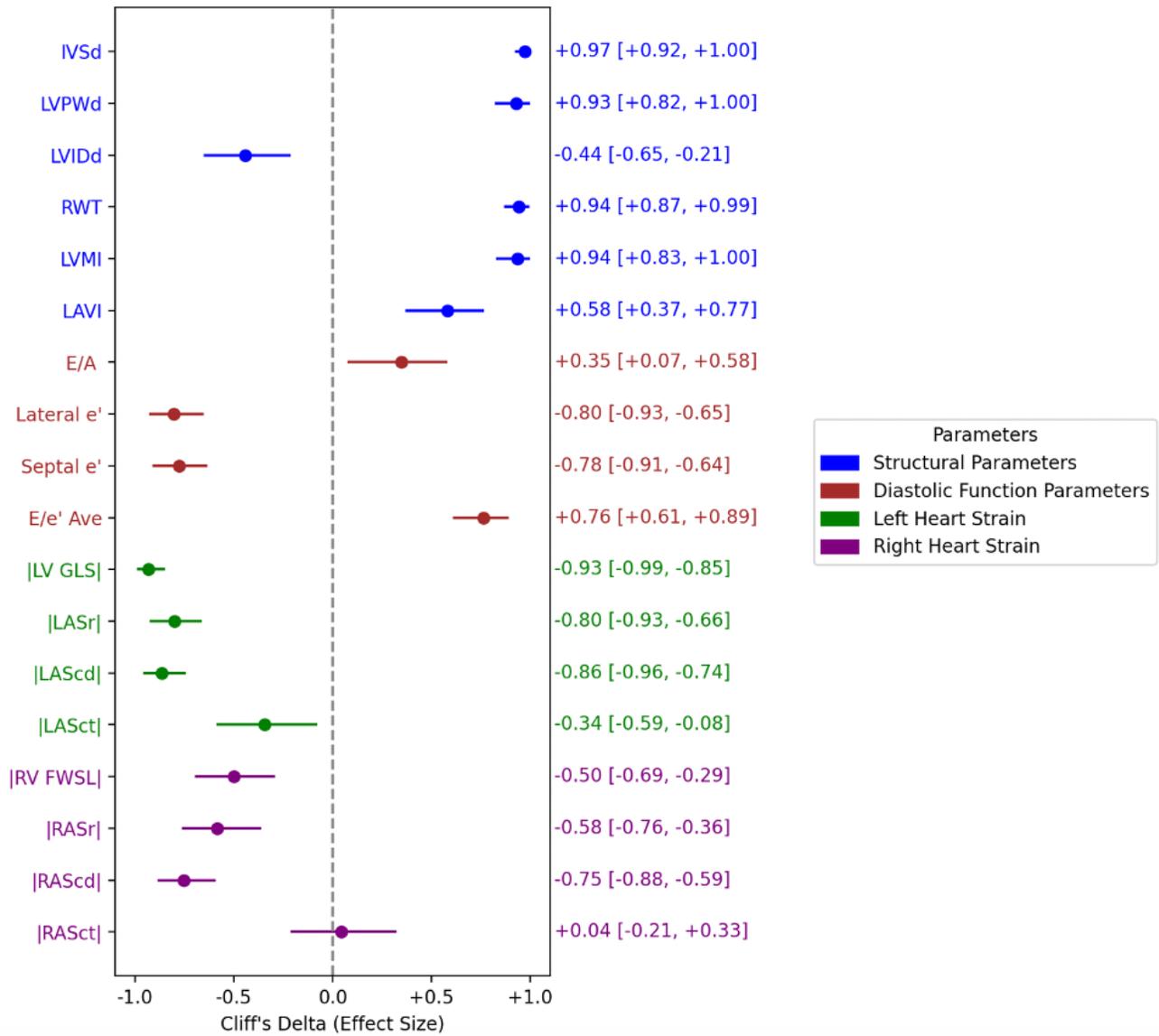
C. Cohort without baseline PYP scan



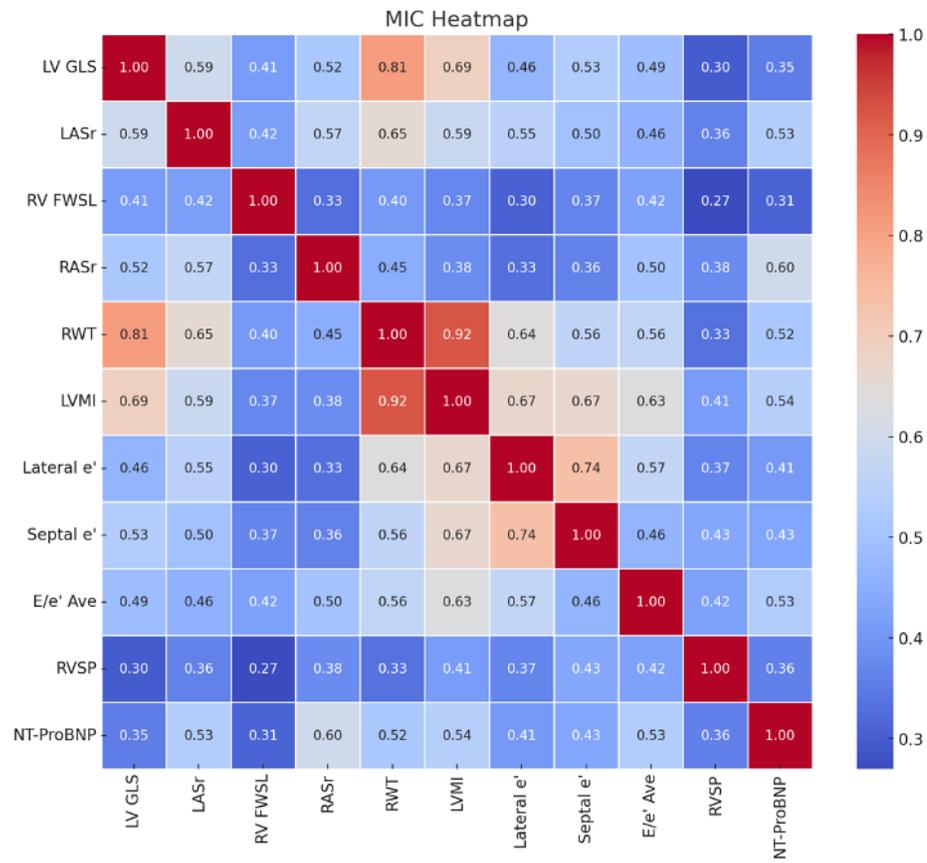
D. Cohort >40 years old



Supplementary Figure 2: Complete analysis of ATTRv-CM patients vs. TTR variant Carriers (including the age-dependent diastolic parameters).



Supplemental Figure 3: MIC scores between nodes; a comprehensive heatmap.



Supplementary Table 2: Baseline echocardiographic characteristics of TTR variant carriers with follow-up information.

Echocardiographic Parameter	Group progressing to ATTR-CM (n=4) ^a	Group free of ATTR-CM (n=22)
	Median [IQR 25,75]	Median [IQR 25,75]
IVSd, cm	0.90 [0.83, 0.98]	0.78 [0.715, 0.945]
LVPWd, cm	0.90 [0.82, 0.99]	0.79 [0.705, 0.9275]
LVIDd, cm	4.65 [4.13, 5.1]	4.6 [4.4, 5.07]
Relative Wall Thickness (RWT)	0.40 [0.32, 0.48]	0.34 [0.30, 0.39]
LV mass index (LVMI), g/m ²	68.82 [66.25, 71.63]	59.97 [54.33, 70.62]
E/A	0.96 [0.89, 1.12]	1.15 [0.96, 1.29]
Lateral e' (cm/s)	8.40 [7.38, 9.58]	9.9 [8.7, 11.2]
Septal e' (cm/s)	6.95 [6.15, 7.75]	8.16 [6.2, 9.8]
E/e' Average	8.6 [7.6, 9.8]	8.7 [6.5, 9.4]
LA volume index (LAVI), ml/m ²	31.6 [27.81, 32.54]	29.52 [21.8, 35.22]
LV Global Longitudinal Strain (GLS), %	-20.2 [-21.6, -18.9]	-21.7 [-23.45, -20.6]
LA reservoir strain (LASr), %	33.7 [31.74, 35.41]	30.85 [27.6, 38.8]
LA conduit strain (LAScd), %	-19.08 [-22.85, -16.65]	-21.2 [-24.25, -15.8]
LA contraction strain (LASct), %	-13.85 [-15.35, -11.55]	-11.8 [-14.4, -8.3]
RV free wall longitudinal strain (RV FWLS), %	-23.6 [-24.33, -22.83]	-26.5 [-27.8, -22.3]
RA reservoir strain (RASr), %	33.95 [32.47, 38.1]	30.3 [25.4, 37.7]
RA conduit strain (RAScd), %	-24.65 [-29.1, -21.55]	-20.4 [-29.1, -17.9]
RA contraction strain (RASct), %	-9.4 [-9.98, -9.08]	-9.2 [-14.8, -5.4]

^aNon-significant differences ($p > 0.05$) between the two groups.