SUPPLEMENTAL MATERIAL

Table A: Myocardial Matrix Biomarker Profiles in Referent Control Subjects, Subjects with Left Ventricular Hypertrophy, and Subjects with Diastolic Heart Failure

	Patient Grouping			F (χ^2)	p-Value
	Referent Control	LVH	DHF		
MMP-1, ng/mL	0.78 ± 0.06	0.89 ± 0.07	0.94 ± 0.17	1.1	0.325
	0.55[0.26,1.05]	0.72[0.37,1.22]	0.67[0.38,1.29]		
MMP-2, ng/mL	339.7 ± 9.3	326.4 ± 11.8	421.4 ± 21.6*†	9.6	<0.001
	328.1[216.4,436.4]	342.2[244.6,421.1]	406.4[312.6,506.2]		
MMP-3, ng/mL	10.08 ± 0.39	9.33 ± 0.42	11.47 ± 0.74†	3.0	0.049
	8.63[6.39,12.11]	8.65[6.01,12.14]	10.79[7.0,14.5]		
MMP-7, ng/mL	1.65 ± 0.08	1.84 ± 0.10	2.14 ± 0.18*	4.2	0.016
	1.29[0.86, 2.10]	1.65[0.97,2.65]	1.2[1.12,2.94]		
MMP-8, ng/mL	2.63 ± 0.22	3.29 ± 0.32	1.79 ± 0.18†	4.4	0.014
	1.11[0.61,2.82]	1.52[0.89,3.30]	1.28[0.89,2.19]		
MMP-9, ng/mL	95.0 ± 3.8	126.7 ± 7.2*	123.8 ± 8.6*	10.7	<0.001
	83.1[53.0,123.3]	104.1[71.2,164.9]	104.1[73.8,161.0]		
TIMP-1, ng/mL	72.2 ± 1.4	82.5 ± 2.1*	90.3 ± 3.4*	18.5	<0.001
	67.8[54.4,88.2]	82.7[64.8,102.6]	84.6[68.5,107.5]		
TIMP-2, ng/mL	78.6 ± 0.9	83.6 ± 1.1*	85.3 ± 1.6*	8.9	<0.001
	79.0[68.46,88.78]	84.62[75.0,93.3]	85.0[77.8,93.3]		
TIMP-3, ng/mL	7.5 ± 0.5	9.2 ± 0.8	6.6 ± 0.9	2.8	0.063
	4.18[1.95,11.69]	5.81[2.29,11.09]	3.66[2.16,7.56]		
TIMP-4, ng/mL	1.47 ± 0.04	1.46 ± 0.05	1.85 ± 0.09*†	8.9	<0.001
	1.33[1.09,1.77]	1.42[1.09,1.89]	1.75[1.28,2.33]		
PINP, ng/mL	37.1 ± 1.3	34.5 ± 1.9	39.4 ± 4.0	1.1	0.327
	32.8[22.6,47.0]	30.2[21.0,42.7]	30.9[22.5,45.7]		
PIIINP, ng/mL	7.2 ± 0.1	7.6 ± 0.2	9.1 ± 0.4*†	18.4	<0.001
	7.12[5.92,8.18]	7.59[6.45,9.31]	8.40[6.75,10.67]		
CITP, ng/mL	3.01 ± 0.12	3.56 ± 0.17	3.93 ± 0.42*	5.0	0.007
	2.90[2.00,3.86]	3.22[2.04,4.71]	3.10[1.83,5.18]		
Cardiotrophin-1, ng/mL10^{-3}	51.1 ± 6.9	43.3 ± 6.8	22.8 ± 5.7	2.4	0.096
	12.09[6.59,40.00]	13.98[5.65,40.00]	10.0[02.92,23.92]		
sRAGE, ng/mL	3.46 ± 0.17	3.15 ± 0.25	2.97 ± 0.27	1.2	0.315
	2.54[1.76,4.18]	2.07[1.50,3.57]	2.25[1.61,3.72]		
Osteopontin, ng/mL	76.2 ± 1.9	86.5 ± 4.7*	92.6 ± 5.5*	5.1	0.007
	73.7[58.8,94.6]	79.9[61.6,102.2]	91.9[66.4,118.9]		
NT-proBNP, pg/m	87.4 ± 6.4	109.4 ± 12.4	214.2 ± 33.6*†	17.7	<0.001
	55.6[29.0,111.8]	75.6[33.8,153.1]	133.1[51.3,302.5]		
Sample Size, n	241	144	61		

Abbreviations:
The table presents means ± standard errors on the first line, and medians ± inter quartile range on the second line. ANOVA F-tests and p-values are reported for $\log_{10}$ biomarker values and post hoc pairwise statistical comparisons were performed.

LVH = patients with left ventricular hypertrophy but no heart failure, DHF = patients with left ventricular hypertrophy and diastolic heart failure, MMP = matrix metalloproteinase, TIMP = tissue inhibitor of MMP, NT-proBNP = n-terminal propeptides of brain naturetic peptide, sRAGE = soluble receptor for advanced glycation endproduct, PINP = n-terminal collagen I propeptide, PIIINP = n-terminal collagen III propeptide, CITP = collagen I telopeptide.

* = $p<0.05$ compared to Referent Control
† = $p<0.05$ compared to LVH

<u>Table B</u>: Effect size (beta), Wald T statistics, and p-value for adjusted models obtained by setting forward variable selection entry criteria at 0.10.

	Biomarker	Beta	Wald T-statistic	p-value
LVH	MMP-7	0.153	3.01	0.080
	MMP-9	0.006	12.04	< 0.001
	TIMP-1	0.018	13.01	< 0.001
	NT-proBNP	0.002	3.37	0.070
	PIIINP	0.113	4.39	0.040
DHF	MMP-2	0.002	3.98	0.050
	MMP-8	-0.247	7.81	0.005
	PIIINP	0.150	3.50	0.002
	TIMP-4	0.818	9.43	0.060

Abbreviations:
LVH = patients with left ventricular hypertrophy, DHF = patients with left ventricular hypertrophy and diastolic heart failure, MMP = matrix metalloproteinase, TIMP = tissue inhibitor of MMP, NT-proBNP = n-terminal propeptides of brain naturetic peptide, PIIINP = n-terminal collagen III propeptide.

Table C: Multivariate, Multi-Biomarker Analysis for LVH and DHF Detection

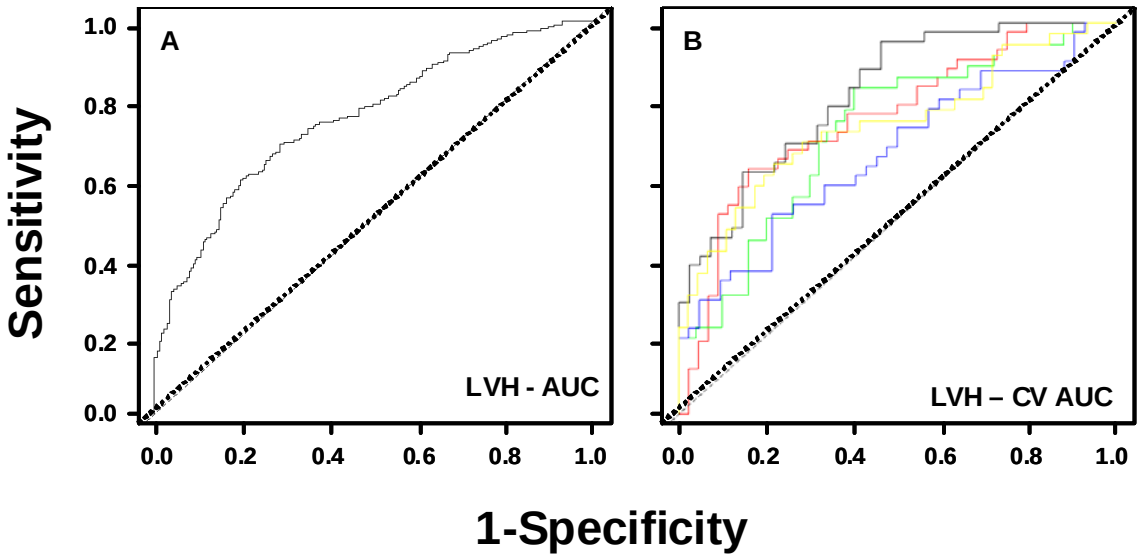
LVH

Algorithm	1 factor	2 factor	3 factor	4 factor	5 factor	NT-pro BNP
AUC [95%CI]	0.65[0.60,0.70]	0.68[0.63,0.73]	0.69[0.64,0.74]	0.69[0.64,0.74]	0.70[0.65,0.75]	0.57[0.52,0.63]
CV AUC	0.65[0.60,0.71]	0.68[0.62,0.74]	0.69[0.63,0.74]	0.68[0.62,0.74]	0.68[0.64, 0.76]	0.58[0.51,0.64]
TIMP-1	X	X	X	X	X	
MMP-9		X	X	X	X	
PIIINP			X X	X	X	
NT-proBNP				X	X	
TIMP-2					X	

DHF

Algorithm	1 factor	2 factor	3 factor	4 factor	NT-pro BNP
AUC	0.68[0.60, 0.76]	0.70[0.62, 0.78]	0.76[0.68, 0.82]	0.77[0.70, 0.84]	0.65[0.56, 0.74]
CV AUC	0.68[0.58, 0.78]	0.69[0.59, 0.79]	0.74[0.64, 0.82]	0.75 [0.67, 0.83]	0.65[0.54, 0.75]
MMP-2	X	X	X	X	
TIMP-4		X	X	X	
MMP-8			X	X	
PIIINP				X	

Abbreviations:
LVH = patients with left ventricular hypertrophy, DHF = patients with left ventricular hypertrophy and diastolic heart failure, MMP = matrix metalloproteinase, TIMP = tissue inhibitor of MMP, NT-proBNP = n-terminal propeptides of brain naturetic peptide, PIIINP = n-terminal collagen III propeptide, AUC = area under the curve (with 95% confidence intervals), CV = cross validated

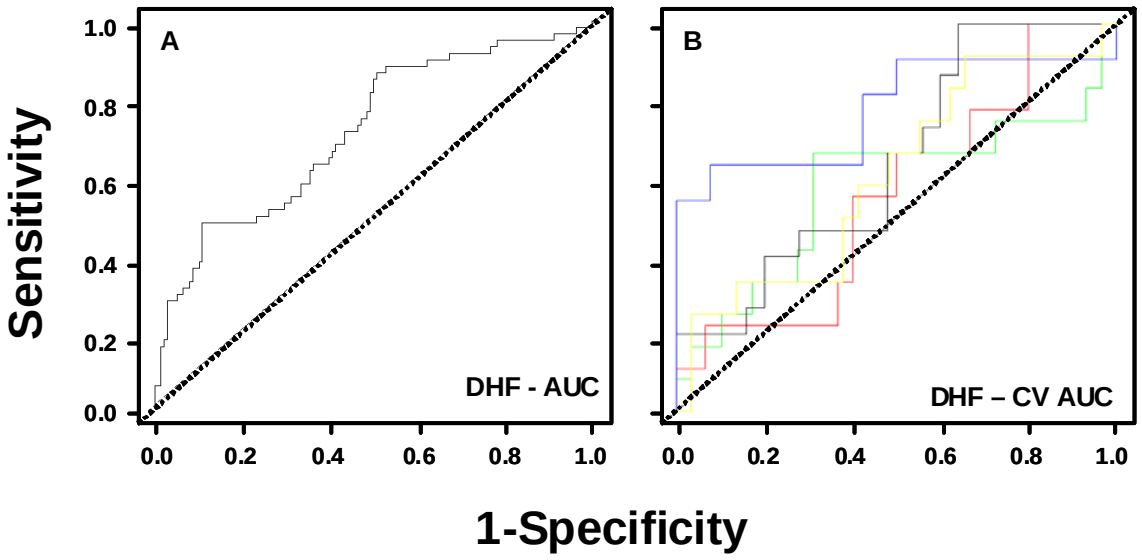


Supplement Figure A

Figure Legend for Supplemental Figure A:

Panel A: Receiver operator curve analysis for plasma NT-proBNP in left ventricular hypertrophy (LVH). Observed area under the curve (AUC) for LVH using clinical covariates plus NT-proBNP = 0.75 [0.71, 0.80].

Panel B: Cross-validated analysis for NT-proBNP in LVH. The ROC curves generated from a 30 random simulated simulations of a 5-fold split of the data are presented. The cross validated ROC curves are similar in shape to those obtained in Panel A.



Supplement Figure B

Figure Legend for Supplemental Figure B:

Panel A: Receiver operator curve analysis for NT-proBNP in diastolic heart failure (DHF). Observed area under the curve (AUC) for DHF using clinical covariates plus NT-proBNP = 0.71 [0.63, 0.79].

Panel B: The ROC curves generated from 30 random simulated simulations of a 5-fold split of the data are presented. The cross-validated ROC curves are similar in shape to those obtained in Panel A.