

# **SUPPLEMENTAL MATERIAL**

**Table S1.** Predictors of the composite event in multivariable analysis models.

Variable	Adjusted Analyses											
	Model 0				Model A – Maximum LA				Model B – Minimum LA			
	n= 359			volume			volume			volume		
	n= 354			n= 354			n= 354			n=336		
Variable	HR	95% CI	P values	HR	95% CI	P values	HR	95% CI	P values	HR	95% CI	P values
Age, years	1.02	0.99-1.04	0.18	1.02	0.99-1.04	0.16	1.02	0.99-1.04	0.17	1.02	0.99-1.04	0.19
Sex, male	0.66	0.40-1.09	0.10	0.68	0.41-1.11	0.12	0.68	0.41-1.12	0.13	<b>0.54</b>	<b>0.32-0.94</b>	<b>0.028</b>
LV ejection fraction, %	<b>0.95</b>	<b>0.93-0.97</b>	<b>&lt;0.0001</b>	<b>0.95</b>	<b>0.93-0.97</b>	<b>&lt;0.0001</b>	<b>0.95</b>	<b>0.93-0.97</b>	<b>&lt;0.0001</b>	<b>0.95</b>	<b>0.92-0.97</b>	<b>&lt;0.0001</b>
E/E' ratio	<b>1.05</b>	<b>1.01-1.09</b>	<b>0.015</b>	<b>1.04</b>	<b>1.00-1.08</b>	<b>0.039</b>	<b>1.04</b>	<b>1.00-1.08</b>	<b>0.044</b>	1.04	0.99-1.08	0.10
RV S', cm/s	0.95	0.86-1.05	0.32	0.95	0.86-1.05	0.30	0.95	0.86-1.05	0.31	1.00	0.90-1.11	0.99
Hypertension	0.60	0.35-1.02	0.058	<b>0.57</b>	<b>0.33-0.97</b>	<b>0.038</b>	<b>0.57</b>	<b>0.33-0.97</b>	<b>0.04</b>	<b>0.50</b>	<b>0.29-0.87</b>	<b>0.014</b>
Cardiac device	0.95	0.56-1.59	0.84	0.95	0.57-1.60	0.18	0.95	0.56-1.59	0.84	0.94	0.54-1.63	0.83
CD cardiac form	<b>6.69</b>	<b>1.56-28.7</b>	<b>0.01</b>	<b>6.42</b>	<b>1.49-27.6</b>	<b>0.01</b>	<b>6.38</b>	<b>1.48-27.4</b>	<b>0.01</b>	<b>6.25</b>	<b>1.45-26.9</b>	<b>0.014</b>
<b>Variable of Interest</b>	-	-	-	1.01	0.99-1.02	0.41	1.01	0.99-1.02	0.32	1.02	0.99-1.04	0.16

CD, Chagas disease; E, peak early wave diastolic filling velocity; E', peak early diastolic mitral annulus velocity; HR, hazard ratio; LA, left atrial; LV, left ventricular; RV, right ventricular; S', peak systolic mitral annulus velocity.

**Table S2.** Predictors of the composite event in multivariable analysis models.

Variable	Adjusted Analyses											
	Model D- 3D LV end-diastolic			Model E – 3D LV end-systolic			Model F – 3D LV ejection			Model G - LASct		
	volume			volume			fraction			n= 341		
	n= 338			n=338			n=338					
Variable	HR	95% CI	P values	HR	95% CI	P values	HR	95% CI	P values	HR	95% CI	P values
Age, years	1.03	0.99-1.05	0.055	1.02	1.00-1.05	0.069	1.02	1.00-1.05	0.06	1.02	1.00-1.05	0.09
Sex, male	0.57	0.32-1.02	0.058	0.67	0.38-1.18	0.16	0.77	0.45-1.32	0.34	<b>0.58</b>	<b>0.34-1.00</b>	<b>0.0498</b>
LV ejection fraction, %	<b>0.95</b>	<b>0.93-0.98</b>	<b>0.0001</b>	<b>0.95</b>	<b>0.93-0.98</b>	<b>0.001</b>	<b>0.94</b>	<b>0.91-0.97</b>	<b>0.0003</b>	<b>0.95</b>	<b>0.92-0.97</b>	<b>&lt;0.0001</b>
E/E' ratio	1.02	0.97-1.07	0.44	1.03	0.99-1.08	0.17	<b>1.05</b>	<b>1.01-1.09</b>	<b>0.02</b>	1.03	0.99-1.08	0.17
RV S', cm/s	0.96	0.87-1.06	0.40	0.95	0.86-1.05	0.35	0.94	0.85-1.05	0.29	1.03	0.92-1.14	0.62
Hypertension	0.64	0.36-1.11	0.11	0.67	0.38-1.17	0.16	0.64	0.37-1.14	0.13	<b>0.53</b>	<b>0.31-0.92</b>	<b>0.0249</b>
Cardiac device	0.80	0.45-1.41	0.44	0.79	0.45-1.39	0.41	0.82	0.46-1.46	0.50	0.97	0.56-1.67	0.91
CD cardiac form	<b>6.07</b>	<b>1.40-26.2</b>	<b>0.016</b>	<b>6.14</b>	<b>1.42-26.5</b>	<b>0.015</b>	<b>5.95</b>	<b>1.38-25.7</b>	<b>0.017</b>	<b>6.21</b>	<b>1.44-26.8</b>	<b>0.014</b>
<b>Variable of Interest</b>	<b>1.01</b>	<b>1.00-1.02</b>	<b>0.019</b>	1.01	0.99-1.02	0.21	1.01	0.97-1.04	0.75	<b>1.09</b>	<b>1.01-1.18</b>	<b>0.026</b>

3D, three dimensional; CD, Chagas disease; E, peak early wave diastolic filling velocity; E', peak early diastolic mitral annulus velocity; HR, hazard ratio; LA, left atrial; LASct, peak negative global LA strain; LV, left ventricular; RV, right ventricular; S', peak systolic mitral annulus velocity.

**Table S3.** Predictors of the composite event in multivariable analysis models.

Adjusted Analyses												
	Model H- LAScd			Model I – LASr			Model J – LV-GLS			Model K - LV-GCS		
Variable	n= 359			n= 359			n= 354			n= 347		
Variable	HR	95% CI	P values	HR	95% CI	P values	HR	95% CI	P values	HR	95% CI	P values
Age, years	1.02	0,99-1.04	0.19	<b>1.01</b>	<b>0.99-1.04</b>	<b>0.30</b>	1.02	0.99-1.04	0.11	1.02	0.99-1.04	0.16
Sex, male	0.66	0.40-1.09	0.11	0.67	0.41-1.04	0.09	0.68	0.41-1.14	0.14	<b>0.61</b>	<b>0.37-0.99</b>	<b>0.049</b>
LV ejection fraction, %	<b>0.95</b>	<b>0.93-0.97</b>	<b>&lt;0.0001</b>	<b>0.95</b>	<b>0.93-0.98</b>	<b>0.0001</b>	<b>0.94</b>	<b>0.91-0.98</b>	<b>0.001</b>	0.98	0.95-1.00	0.09
E/E' ratio	<b>1.05</b>	<b>1.01-1.09</b>	<b>0.01</b>	1.04	0.99-1.08	0.05	<b>1.05</b>	<b>1.01-1.09</b>	<b>0.019</b>	1.04	1.00-1.08	0.057
RV S', cm/s	0.95	0.86-1.05	0.32	0.97	0.87-1.07	0.51	0.94	0.85-1.05	0.28	0.98	0.88-1.08	0.70
Hypertension	0.60	0.35-1.02	0.06	0.59	0.34-1.00	0.049	<b>0.58</b>	<b>0.34-0.98</b>	<b>0.04</b>	0.71	0.40-1.23	0.22
Cardiac device	0.95	0.56-1.59	0.84	0.95	0.57-1.59	0.85	0.99	0.58-1.70	0.99	0.86	0.50-1.47	0.59
CD cardiac form	<b>6.70</b>	<b>1.56-28.7</b>	<b>0.01</b>	<b>6.38</b>	<b>1.48-27.4</b>	<b>0.01</b>	<b>6.43</b>	<b>1.50-27.6</b>	<b>0.01</b>	<b>5.74</b>	<b>1.33-24.7</b>	<b>0.019</b>
<b>Variable of Interest</b>	1.00	0.93-1.08	0.90	0.97	0.92-1.02	0.24	0.98	0.88-1.09	0.98	<b>1.13</b>	<b>1.04-1.21</b>	<b>0.002</b>

CD, Chagas disease; E, peak early wave diastolic filling velocity; E', peak early diastolic mitral annulus velocity; GCS, global circumferential strain; GLS, global longitudinal strain; HR, hazard ratio; LA, left atrial; LAScd, peak positive global LA strain; LASr, total global LA strain; LV, left ventricular; RV, right ventricular; S', peak systolic mitral annulus velocity.

**Table S4.** Predictors of the composite event in multivariable analysis models.

Adjusted Analyses												
Variable	Model L- LV-GRS			Model M – Peak Twist			Model N – Peak Torsion			Model O - RV-fwLS		
	n= 347	n= 334	n = 334	n= 337								
Variable	HR	95% CI	P values	HR	95% CI	P values	HR	95% CI	P values	HR	95% CI	P values
Age, years	1.02	0.99-1.04	0.17	1.02	0.99-1.04	0.22	1.02	0.99-1.04	0.19	1.02	0.99-1.04	0.18
Sex, male	0.65	0.40-1.08	0.10	0.66	0.40-1.08	0.10	0.62	0.38-1.03	0.06	0.65	0.38-1.11	0.11
LV ejection fraction, %	<b>0.95</b>	<b>0.93-0.98</b>	<b>0.0001</b>	<b>0.95</b>	<b>0.93-0.98</b>	<b>&lt;0.0001</b>	<b>0.96</b>	<b>0.94-0.98</b>	<b>0.0002</b>	<b>0.95</b>	<b>0.93-0.97</b>	<b>&lt;0.0001</b>
E/E' ratio	<b>1.04</b>	<b>1.00-1.09</b>	<b>0.027</b>	1.04	0.99-1.08	0.09	1.04	0.99-1.08	0.10	<b>1.05</b>	<b>1.01-1.10</b>	<b>0.01</b>
RV S', cm/s	0.96	0.86-1.06	0.43	0.95	0.86-1.06	0.36	0.95	0.86-1.06	0.35	0.95	0.86-1.06	0.38
Hypertension	<b>0.58</b>	<b>0.34-1.00</b>	<b>0.049</b>	0.71	0.41-1.25	0.24	0.72	0.41-1.27	0.26	0.58	0.33-1.02	0.057
Cardiac device	0.91	0.53-1.56	0.73	0.83	0.48-1.44	0.51	0.81	0.47-1.42	0.47	1.04	0.60-1.80	0.90
CD cardiac form	<b>6.45</b>	<b>1.50-27.8</b>	<b>0.01</b>	<b>5.08</b>	<b>1.17-22.0</b>	<b>0.03</b>	<b>4.86</b>	<b>1.12-21.1</b>	<b>0.03</b>	<b>12.2</b>	<b>1.63-91.9</b>	<b>0.01</b>
Variable of Interest	0.99	0.97-1.02	0.67	<b>0.94</b>	<b>0.90-0.99</b>	<b>0.02</b>	<b>0.56</b>	<b>0.37-0.85</b>	<b>0.006</b>	0.97	0.92-1.02	0.23

CD, Chagas disease; E, peak early wave diastolic filling velocity; E', peak early diastolic mitral annulus velocity; GRS, global radial strain; HR, hazard ratio; LV, left ventricular; RV, right ventricular; RV-fwLS, RV free wall longitudinal strain; S', peak systolic mitral annulus velocity.

**Table S5.** Predictors of the composite event in multivariable analysis models.

Adjusted Analyses												
Variable	Model P- Troponin I			Model Q – BNP			Model R – TGF-β1			Model S - TNF		
	n= 315	n= 335	n = 313	n= 329								
Age, years	1.02	0.99-1.04	0.16	1.01	0.99-1.04	0.29	1.01	0.99-1.04	0.28	1.01	0.99-1.04	0.23
Sex, male	0.70	0.41-1.17	0.17	0.68	0.41-1.13	0.14	0.73	0.43-1.25	0.25	0.65	0.39-1.08	0.10
LV ejection fraction, %	<b>0.96</b>	<b>0.93-0.98</b>	<b>0.0001</b>	<b>0.95</b>	<b>0.93-0.97</b>	<0.0001	<b>0.95</b>	<b>0.93-0.98</b>	<b>0.0001</b>	<b>0.95</b>	<b>0.93-0.97</b>	<0.0001
E/E' ratio	<b>1.05</b>	<b>1.00-1.10</b>	<b>0.03</b>	1.04	1.00-1.08	0.06	<b>1.05</b>	<b>1.00-1.10</b>	<b>0.03</b>	<b>1.05</b>	<b>1.01-1.09</b>	<b>0.01</b>
RV S', cm/s	0.94	0.85-1.04	0.25	0.93	0.84-1.02	0.13	0.94	0.84-1.05	0.26	0.96	0.86-1.06	0.40
Hypertension	0.59	0.34-1.02	0.058	0.72	0.42-1.23	0.23	0.69	0.40-1.21	0.20	0.63	0.37-1.08	0.10
Cardiac device	1.00	0.58-1.70	0.99	0.85	0.50-1.44	0.55	0.86	0.49-1.50	0.59	0.90	0.53-1.53	0.70
CD cardiac form	<b>6.51</b>	<b>1.51-28.0</b>	<b>0.01</b>	<b>6.85</b>	<b>1.60-29.3</b>	<b>0.009</b>	<b>6.84</b>	<b>1.59-29.4</b>	<b>0.0097</b>	<b>7.05</b>	<b>1.65-30.2</b>	<b>0.008</b>
<b>Variable of Interest</b>	0.99	0.83-1.16	0.88	1.94	0.99-3.82	0.05	0.99	0.97-1.01	0.51	1.02	0.97-1.06	0.48

BNP, brain natriuretic peptide; CD, Chagas disease; E, peak early wave diastolic filling velocity; E', peak early diastolic mitral annulus velocity; HR, hazard ratio; LV, left ventricular; RV, right ventricular; S', peak systolic mitral annulus velocity; TGF-β1, transforming growth factor β1; TNF, tumor necrosis factor.

**Table S6.** Predictors of the composite event in multivariable analysis models.

Adjusted Analyses												
Variable	Model T- MMP-2			Model U- MMP-9			Model V – <i>T. cruzi</i> PCR			Model X – Parasitic load		
	n= 335			n= 332			n= 331			n = 331		
Variable	HR	95% CI	P values	HR	95% CI	P values	HR	95% CI	P values	HR	95% CI	P values
Age, years	1.01	0.99-1.04	0.28	1.01	0.99-1.04	0.28	1.03	0.99-1.06	0.06	1.02	1.00-1.05	0.07
Sex, male	0.64	0.39-1.07	0.09	0.67	0.41-1.12	0.13	0.75	0.44-1.26	0.27	0.72	0.42-1.21	0.21
LV ejection fraction, %	<b>0.95</b>	<b>0.93-0.97</b>	<b>&lt;0.0001</b>	<b>0.95</b>	<b>0.93-0.97</b>	<b>&lt;0.0001</b>	<b>0.94</b>	<b>0.92-0.96</b>	<b>&lt;0.0001</b>	<b>0.95</b>	<b>0.93-0.97</b>	<b>&lt;0.0001</b>
E/E' ratio	1.05	1.01-1.09	0.018	1.05	1.01-1.09	0.02	1.04	1.00-1.08	0.07	1.04	0.99-1.08	0.08
RV S', cm/s	0.95	0.86-1.04	0.27	0.95	0.86-1.05	0.32	0.95	0.86-1.05	0.33	0.95	0.86-1.05	0.30
Hypertension	0.64	0.37-1.08	0.09	0.65	0.38-1.12	0.12	0.59	0.34-1.02	0.06	<b>0.57</b>	<b>0.33-0.99</b>	<b>0.048</b>
Cardiac device	0.89	0.52-1.50	0.65	0.93	0.54-1.60	0.79	0.77	0.43-1.37	0.38	0.84	0.47-1.49	0.55
CD cardiac form	<b>6.79</b>	<b>1.59-29.0</b>	<b>0.0098</b>	<b>6.85</b>	<b>1.60-29.3</b>	<b>0.009</b>	<b>6.04</b>	<b>1.41-26.0</b>	<b>0.02</b>	<b>6.59</b>	<b>1.53-28.3</b>	<b>0.01</b>
Variable of Interest	1.01	0.97-1.06	0.51	1.02	0.94-1.07	0.95	<b>1.77</b>	<b>1.09-2.86</b>	<b>0.02</b>	1.01	0.98-1.03	0.55

CD, Chagas disease; E, peak early wave diastolic filling velocity; E', peak early diastolic mitral annulus velocity; HR, hazard ratio; LV, left ventricular; MMP, matrix metalloproteinase; PCR, polymerase chain reaction; RV, right ventricular; S', peak systolic mitral annulus velocity; *T. cruzi*, *Trypanosoma cruzi*.

**Table S7.** Predictors of the composite event in multivariable analysis models adjusted for competing risks.

Variable	Adjusted Analyses											
	3D LV end-diastolic volume				LASct				LV-GCS			Peak Twist
	n= 338			n= 341			n= 347			n= 334		
Variable	HR	95% CI	P values	HR	95% CI	P values	HR	95% CI	P values	HR	95% CI	P values
Age, years	1.01	0.99-1.04	0.31	<b>1.01</b>	<b>1.00-1.17</b>	<b>0.04</b>	1.01	0.98-1.03	0.63	1.01	0.98-1.03	0.60
Sex, male	0.56	0.31-1.02	0.059	0.58	0.34-1.00	0.051	0.61	0.36-1.03	0.067	0.65	0.39-1.06	0.09
LV ejection fraction, %	<b>0.96</b>	<b>0.94-0.98</b>	<b>&lt;0.001</b>	<b>0.95</b>	<b>0.93-0.97</b>	<b>&lt;0.001</b>	0.98	0.95-1.00	0.08	<b>0.96</b>	<b>0.94-0.98</b>	<b>&lt;0.001</b>
E/E' ratio	1.02	0.97-1.07	0.36	<b>1.04</b>	<b>1.00-1.08</b>	<b>0.049</b>	<b>1.04</b>	<b>1.00-1.08</b>	<b>0.03</b>	1.04	1.00-1.08	0.06
RV S', cm/s	0.95	0.86-1.06	0.38	1.01	0.93-1.11	0.76	0.98	0.87-1.10	0.68	0.95	0.85-1.06	0.37
Hypertension	0.75	0.43-1.29	0.43	0.66	0.38-1.15	0.14	0.83	0.45-1.52	0.54	0.82	0.47-1.45	0.50
Cardiac device	0.74	0.41-1.32	0.31	0.89	0.52-1.54	0.69	0.81	0.47-1.38	0.44	0.76	0.44-1.34	0.35
CD cardiac form	<b>6.17</b>	<b>1.39-27.3</b>	<b>0.017</b>	<b>6.39</b>	<b>1.45-28.2</b>	<b>0.014</b>	<b>5.86</b>	<b>1.31-26.3</b>	<b>0.02</b>	<b>5.06</b>	<b>1.10-23.3</b>	<b>0.037</b>
Variable of Interest	<b>1.01</b>	<b>1.00-1.02</b>	<b>0.024</b>	<b>1.08</b>	<b>1.00-1.17</b>	<b>0.04</b>	<b>1.12</b>	<b>1.04-1.21</b>	<b>0.003</b>	<b>0.94</b>	<b>0.89-0.99</b>	<b>0.01</b>

3D, three-dimensional; CD, Chagas disease; E, peak early wave diastolic filling velocity; E', peak early diastolic mitral annulus velocity; GCS, global circumferential strain; HR, hazard ratio; LA, left atrial; LASct, peak negative global LA strain; LV, left ventricular; RV, right ventricular; S', peak systolic mitral annulus velocity.

**Table S8.** Predictors of the composite event in multivariable analysis models adjusted for competing risks.

Variable	Adjusted Analyses								
	Peak Torsion			BNP			<i>T. cruzi</i> PCR		
	n = 334			n= 335			n= 331		
	HR	95% CI	P values	HR	95% CI	P values	HR	95% CI	P values
Age, years	1.01	0.98-1.03	0.54	1.00	0.98-1.03	0.75	1.02	0.99-1.04	0.18
Sex, male	0.61	0.37-1.03	0.057	0.69	0.41-1.15	0.15	0.80	0.48-1.33	0.39
LV ejection fraction, %	<b>0.95</b>	<b>0.94-0.98</b>	<b>&lt;0.001</b>	<b>0.95</b>	<b>0.93-0.97</b>	<b>&lt;0.001</b>	<b>0.95</b>	<b>0.93-0.97</b>	<b>&lt;0.001</b>
E/E' ratio	1.04	1.00-1.08	0.066	<b>1.04</b>	<b>1.01-1.08</b>	<b>0.02</b>	<b>1.04</b>	<b>1.01-1.08</b>	<b>0.02</b>
RV S', cm/s	0.95	0.85-1.06	0.37	0.92	0.83-1.02	0.10	0.95	0.85-1.05	0.28
Hypertension	0.83	0.47-1.47	0.53	0.85	0.50-1.43	0.54	0.67	0.39-1.15	0.14
Cardiac device	0.75	0.43-1.32	0.32	0.80	0.47-1.36	0.41	0.76	0.44 -1.33	0.34
CD cardiac form	<b>4.85</b>	<b>1.05-22.4</b>	<b>0.04</b>	<b>6.94</b>	<b>1.59-30.3</b>	<b>0.01</b>	<b>5.97</b>	<b>1.35-26.3</b>	<b>0.018</b>
<b>Variable of Interest</b>	<b>0.53</b>	<b>0.35-0.81</b>	<b>0.003</b>	<b>2.03</b>	<b>1.23-3.35</b>	<b>0.005</b>	<b>1.80</b>	<b>1.12-2.91</b>	<b>0.01</b>

BNP, brain natriuretic peptide; CD, Chagas disease; E, peak early wave diastolic filling velocity; E', peak early diastolic mitral annulus velocity; HR, hazard ratio; LV, left ventricular; PCR, polymerase chain reaction; RV, right ventricular; S', peak systolic mitral annulus velocity; *T. cruzi*, *Trypanosoma cruzi*.