

Supplementary Figure Legends

Supplementary Figure 1 – Proportion of males and females within tertiles of both non-indexed and indexed interventricular septum in diastole (IVSd)

Patients grouped into tertiles based on (a) IVSd when non-indexed, (b) IVSd indexed to body surface area (BSA) and (c) IVSd indexed to height and separated into males and females to determine the relative proportion of patients within each tertile.

Supplementary Table 1 – Echocardiographic findings at baseline in patients with ATTR-CM classified by genotype & subdivided by sex

| Variables | Wild-type (n = 1095) | | | T60A (n = 206) | | | V122I (n = 431) | | |
|------------|-----------------------|-----------------------|------------------|-----------------------|-----------------------|------------------|-----------------------|-----------------------|------------------|
| | Male (n = 1029) | Female (n = 66) | P- value | Male (n = 145) | Female (n = 61) | P- value | Male (n = 311) | Female (n = 120) | P-value |
| IVSd (mm) | 17.16 (2.34) | 15.98 (2.44) | 0.001 | 17.14 (2.76) | 16.09 (3.30) | 0.007 | 17.05 (2.16) | 16.26 (2.41) | 0.003 |
| PWTd (mm) | 16.50 (2.44) | 16.02 (2.39) | 0.150 | 16.66 (2.79) | 15.75 (3.33) | 0.075 | 16.60 (2.38) | 15.95 (2.14) | 0.007 |
| LVM (g) | 320.11 (83.19) | 240.67 (90.94) | <0.001 | 324.24 (92.01) | 252.50 (86.71) | <0.001 | 305.52 (82.30) | 263.92 (69.99) | <0.001 |
| LVEDD (mm) | 44.04 (5.70) | 38.89 (4.96) | <0.001 | 43.91 (5.78) | 40.07 (4.84) | <0.001 | 42.74 (6.19) | 40.29 (5.70) | <0.002 |
| LVESD (mm) | 33.35 (6.15) | 28.69 (5.12) | <0.001 | 31.40 (6.20) | 29.68 (5.38) | 0.051 | 33.60 (6.64) | 30.50 (5.56) | <0.001 |
| MWT (mm) | 16.66 (2.78) | 15.19 (4.23) | 0.001 | 16.43 (3.35) | 15.65 (3.85) | 0.011 | 16.66 (2.68) | 15.97 (2.60) | 0.027 |
| RWT | 0.77 (0.17) | 0.84 (0.16) | 0.008 | 0.77 (0.18) | 0.80 (0.22) | 0.939 | 0.80 (0.19) | 0.81 (0.17) | 0.653 |
| LVEDV (ml) | 80.75 (24.86) | 52.35 (16.59) | <0.001 | 82.33 (28.13) | 64.48 (21.43) | 0.002 | 78.48 (29.26) | 61.54 (22.14) | <0.001 |
| LVESV (ml) | 41.67 (17.10) | 24.80 (11.59) | <0.001 | 41.26 (18.32) | 30.72 (12.56) | <0.001 | 46.14 (22.79) | 33.72 (16.59) | <0.001 |
| SV (ml) | 39.08 (13.15) | 28.00 (8.87) | <0.001 | 41.05 (14.94) | 33.76 (14.03) | 0.046 | 32.40 (11.95) | 27.82 (9.80) | 0.003 |
| EF (%) | 49.04 (10.28) | 53.07 (10.71) | 0.011 | 51.35 (9.78) | 51.44 (10.65) | 0.655 | 42.77 (11.23) | 46.32 (11.60) | 0.004 |

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|------------------------|----------------------|----------------------|------------------|---------------------|---------------------|------------------|---------------------|----------------------|------------------|
| LA diameter (mm) | 45.37 (5.79) | 42.79 (5.30) | 0.005 | 42.03 (5.99) | 39.21 (5.96) | 0.002 | 43.82 (5.72) | 42.76 (5.75) | 0.197 |
| LAA (cm ²) | 26.72 (5.68) | 25.22 (4.61) | 0.069 | 23.88 (5.01) | 21.63 (4.57) | 0.001 | 26.00 (5.39) | 25.54 (4.92) | 0.565 |
| RAA (cm ²) | 25.15 (6.30) | 22.09 (6.85) | <0.001 | 21.45 (5.10) | 16.68 (3.77) | <0.001 | 25.26 (6.78) | 22.51 (5.41) | <0.001 |
| E/A | 2.09 (1.10) | 1.85 (1.05) | 0.307 | 1.62 (0.97) | 1.59 (0.90) | 0.892 | 2.49 (1.05) | 2.26 (1.04) | 0.071 |
| E/e' average | 16.72 (6.28) | 21.54 (8.81) | <0.001 | 16.93 (7.28) | 21.07 (8.72) | 0.062 | 17.10 (5.79) | 19.39 (7.26) | 0.002 |
| MAPSE (mm) | 8.14 (2.56) | 8.34 (2.50) | 0.654 | 8.44 (2.55) | 8.22 (2.59) | 0.938 | 7.38 (2.28) | 7.62 (2.46) | 0.330 |
| TAPSE (mm) | 15.09 (4.91) | 14.79 (5.60) | 0.759 | 16.97 (4.69) | 15.97 (4.16) | 0.806 | 14.48 (4.59) | 14.56 (4.78) | 0.619 |
| RV S' (cm/s) | 10.21 (3.13) | 10.42 (3.86) | 0.423 | 10.61 (2.93) | 10.05 (2.85) | 0.725 | 9.66 (2.79) | 9.91 (3.08) | 0.289 |
| PASP (mmHg) | 37.57 (12.99) | 34.36 (16.20) | 0.043 | 30.17 (16.63) | 30.65 (17.58) | 0.687 | 39.96 (15.25) | 42.21 (13.15) | 0.304 |
| TAPSE/PASP | 0.66 (0.61) | 0.59 (0.73) | 0.613 | 0.66 (0.61) | 0.59 (0.73) | 0.613 | 0.43 (0.50) | 0.39 (0.41) | 0.400 |
| GLS (%) | -11.04 (3.63) | -11.65 (4.13) | 0.252 | -11.63 (3.82) | -12.20 (3.89) | 0.114 | -9.35 (3.06) | -10.67 (3.80) | 0.001 |
| Significant MR | 102 (10.0%) | 8 (12.1%) | 0.584 | 19 (13.1%) | 6 (9.8%) | 0.509 | 67 (21.5%) | 34 (28.3%) | 0.135 |
| Significant TR | 140 (13.7%) | 14 (21.1%) | 0.095 | 9 (6.2%) | 8 (13.1%) | 0.101 | 100 (32.2%) | 37 (30.8%) | 0.780 |

All *P*-values are adjusted for age. Data are presented as means (SD), with the exception of significant MR and TR which are presented as number (%). E/A – mitral inflow E/A ratio, EF – ejection fraction, GLS – global longitudinal strain, IVSd – interventricular systolic wall thickness in diastole, LA – left atrium, LAA – left atrial area, LVEDD – left ventricular end diastolic diameter, LVEDV – left ventricular end diastolic volume, LVESD – left ventricular end systolic diameter, LVESV – left ventricular end systolic volume, LVM – left ventricular mass, MAPSE – mitral annular plane systolic excursion, MR – mitral regurgitation, MWT – mean wall thickness, PASP – pulmonary artery systolic pressure, PWTd – posterior wall thickness in diastole, RAA – right atrial area, RV S' velocity – right ventricle systolic excursion velocity, SV – stroke volume, TAPSE – tricuspid annular plane systolic excursion, TAPSE/PASP – tricuspid annular plane systolic excursion to pulmonary artery systolic pressure ratio, TR – tricuspid regurgitation

Supplementary Table 2 – Echocardiographic findings at baseline indexed to body surface area and height, in patients with ATTR-CM classified by genotype and subdivided by sex

| Variables | Wild-type (n = 1095) | | | T60A (n = 206) | | | V122I (n = 431) | | |
|--|-----------------------|-----------------------|--------------|--------------------|---------------------|--------------|--------------------|--------------------|--------------|
| | Male (n = 1029) | Female (n = 66) | P-value | Male (n = 145) | Female (n = 61) | P-value | Male (n = 311) | Female (n = 120) | P-value |
| IVSd index to BSA (mm/m ²) | 8.87 (1.53) | 9.28 (2.37) | 0.172 | 8.72 (2.03) | 10.10 (2.15) | 0.001 | 8.96 (1.35) | 9.56 (1.92) | 0.002 |
| IVSd indexed for height (mm/m) | 9.67 (1.66) | 9.90 (2.41) | 0.910 | 9.49 (2.10) | 9.98 (2.03) | 0.153 | 9.89 (1.53) | 10.16 (2.06) | 0.209 |
| PWTd index to BSA (mm/m ²) | 8.53 (1.54) | 9.32 (2.33) | 0.001 | 8.50 (2.05) | 9.84 (1.98) | 0.002 | 8.73 (1.45) | 9.37 (1.72) | 0.001 |
| PWTd indexed for height (mm/m) | 9.49 (1.69) | 9.91 (2.40) | 0.193 | 9.27 (2.14) | 9.72 (1.92) | 0.164 | 9.63 (1.65) | 9.96 (1.91) | 0.102 |
| LVM index to BSA (g/m ²) | 166.40 (41.75) | 146.73 (49.63) | 0.004 | 166.90 (47.47) | 162.23 (50.91) | 0.568 | 161.03 (37.61) | 155.18 (40.64) | 0.182 |

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|---|-----------------------|-----------------------|------------------|-----------------------|----------------------|------------------|-----------------------|-----------------------|------------------|
| LVM indexed for height (mm/m) | 185.13 (46.65) | 157.39 (53.85) | <0.001 | 180.08 (56.77) | 156.40 (7.59) | 0.011 | 178.31 (45.57) | 166.09 (45.91) | 0.016 |
| LVEDD index to BSA (mm/m ²) | 22.75 (3.51) | 22.61 (5.20) | 0.807 | 22.53 (4.79) | 25.31 (3.53) | <0.001 | 22.35 (3.72) | 23.52 (4.25) | 0.010 |
| LVESD index to BSA (mm/m ²) | 17.21 (3.46) | 16.61 (4.34) | 0.247 | 16.51 (4.42) | 18.79 (3.78) | 0.001 | 17.54 (3.80) | 17.59 (4.12) | 0.998 |
| MWT index to BSA (mm/m ²) | 8.70 (1.46) | 9.31 (2.32) | 0.010 | 8.69 (2.22) | 9.97 (2.03) | 0.005 | 8.84 (1.33) | 9.47 (1.76) | 0.001 |
| MWT indexed for height (mm/m) | 9.69 (1.56) | 9.91 (2.38) | 0.248 | 9.38 (2.10) | 9.85 (1.94) | 0.552 | 9.76 (1.51) | 10.06 (1.93) | 0.113 |
| LVEDV index to BSA (ml/m ²) | 41.19 (13.06) | 30.26 (11.20) | <0.001 | 41.06 (15.77) | 40.32 (12.30) | 0.855 | 40.61 (14.69) | 35.17 (13.47) | 0.002 |
| LVESV index to BSA (ml/m ²) | 21.22 (8.89) | 14.30 (7.37) | <0.001 | 20.66 (9.96) | 19.34 (8.10) | 0.546 | 23.85 (11.66) | 19.14 (9.77) | <0.001 |
| SV index to BSA (ml/m ²) | 19.97 (6.82) | 16.21 (5.98) | <0.001 | 20.56 (7.98) | 20.97 (7.85) | 0.335 | 16.79 (6.03) | 16.04 (6.27) | 0.456 |

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|--|--------------|--------------|-------|---------------------|---------------------|--------------|---------------------|---------------------|------------------|
| LAA index to BSA (cm ² /m ²) | 13.78 (3.14) | 14.70 (4.06) | 0.081 | 12.23 (3.27) | 13.60 (2.75) | 0.114 | 13.22 (3.75) | 14.90 (3.86) | <0.001 |
| RAA index to BSA (cm ² /m ²) | 12.93 (3.35) | 12.89 (4.85) | 0.523 | 10.96 (3.01) | 10.47 (2.23) | 0.046 | 12.81 (4.22) | 13.09 (3.74) | 0.880 |

All *P*-values are adjusted for age. Data are presented as means (and standard deviation). BSA – body surface area, IVSd – interventricular systolic wall thickness in diastole, LAA – left atrial area, LVEDD – left ventricular end diastolic diameter, LVEDV – left ventricular end diastolic volume, LVESD – left ventricular end systolic diameter, LVESV – left ventricular end systolic volume, MWT – mean wall thickness, PWTd – posterior wall thickness in diastole, RAA – right atrial area, SV – stroke volume

Supplementary Table 3 – Regression coefficient representing the difference in means (males minus females) of echocardiographic variable at 1 year

| Echocardiographic Variable | All patients (n=906; 116 females) | | Wild-type (n=595; 26 females) | | T60A (n=99; 29 females) | | V122I (n=212; 61 females) | |
|----------------------------|-----------------------------------|-----------------|---------------------------------|---------|---------------------------------|-------------|---------------------------------|---------|
| | Regression Coefficient (95% CI) | P-value | Regression Coefficient (95% CI) | P-value | Regression Coefficient (95% CI) | P-value | Regression Coefficient (95% CI) | P-value |
| IVSd index to BSA | -0.20 (-0.33; -0.06) | <0.01 | -0.01 (-0.25; 0.22) | 0.92 | -0.72 (-1.29; -0.14) | 0.02 | -0.09 (-0.26; 0.09) | 0.34 |
| PWTd index to BSA | -0.23 (-0.39; -0.06) | <0.01 | -0.17 (-0.48; 0.13) | 0.27 | -0.45 (-1.03; 0.14) | 0.14 | -0.12 (-0.35; 0.11) | 0.31 |
| MWT index to BSA | -0.17 (-0.32; -0.02) | 0.03 | -0.05 (-0.34; 0.23) | 0.71 | -0.56 (-1.11; 0.002) | 0.05 | -0.06 (-0.22; 0.10) | 0.45 |
| RWT | -0.01 (-0.03; 0.01) | 0.40 | 0 (-0.41; 0.42) | 0.98 | -0.01 (-0.06; 0.05) | 0.84 | -0.01 (-0.04; 0.03) | 0.71 |
| LVEDD index to BSA | -0.33 (-0.77; 0.10) | 0.13 | -0.40 (-1.20; 0.41) | 0.34 | -0.91 (-2.46; 0.63) | 0.24 | -0.22 (-0.83; 0.40) | 0.49 |
| LVESD index to BSA | -0.38 (-0.88; 0.12) | 0.13 | 0.04 (-0.96; 1.04) | 0.94 | -0.63 (-2.20; 0.93) | 0.42 | -0.41 (-1.07; 0.25) | 0.22 |

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|-----------------------------|--------------------------|------------------|---------------------------|-------------|--------------------------|-----------------|--------------------------|--------------|
| LVEDV index to BSA | 3.37 (1.12; 5.63) | <0.01 | 4.43 (0.003; 8.86) | 0.05 | 0.52 (-5.76; 6.79) | 0.87 | 0.84 (-2.33; 4.01) | 0.60 |
| LVESV index to BSA | 1.65 (0.22; 3.07) | 0.02 | 3.15 (0.44; 5.86) | 0.02 | 0.13 (-3.38; 3.63) | 0.94 | 0.70 (-1.74; 3.13) | 0.57 |
| SV index to BSA | 1.69 (0.42; 2.95) | <0.01 | 1.65 (-0.90; 4.21) | 0.21 | 1.73 (-1.56; 5.03) | 0.30 | -0.31 (-1.83; 1.20) | 0.69 |
| EF (%) | -0.81 (-2.58; 0.96) | 0.37 | -3.44 (-6.95; 0.06) | 0.05 | 0.90 (-3.58; 5.38) | 0.69 | -2.00 (-4.74; 0.73) | 0.15 |
| LAD | 2.23 (1.29; 3.16) | <0.001 | 0.85 (-0.99; 2.70) | 0.36 | 3.28 (0.83; 5.74) | <0.01 | 2.23 (0.80; 3.65) | 0.002 |
| LAA 4ch index to BSA | -0.24 (-0.71; 0.22) | 0.30 | -0.69 (-1.60; 0.21) | 0.13 | 0.54 (-0.69; 1.76) | 0.39 | -0.49 (-1.19; 0.21) | 0.17 |
| RAA 4ch index to BSA | 0.14 (-0.35; 0.63) | 0.57 | 0.54 (-0.42; 1.50) | 0.27 | 0.18 (-0.78; 1.14) | 0.72 | 0.37 (-0.49; 1.23) | 0.40 |
| E/A Ratio | -0.01 (-0.23; 0.22) | 0.96 | 0.16 (-0.27; 0.60) | 0.46 | 0.26 (-0.30; 0.82) | 0.35 | -0.17 (-0.50; 0.15) | 0.30 |
| E/e' average | -0.59 (-1.69; 0.50) | 0.29 | -1.49 (-3.71; 0.74) | 0.19 | 3.33 (0.49; 6.17) | 0.02 | -1.07 (-2.48; 0.34) | 0.14 |
| MAPSE | 0.40 (-0.06; 0.86) | 0.09 | 0.10 (-0.78; 0.98) | 0.82 | 0.58 (-0.64; 1.80) | 0.35 | -0.11 (-0.81; 0.58) | 0.75 |
| TAPSE | -0.06 (-0.84; 0.71) | 0.88 | -0.76 (-2.24; 0.71) | 0.31 | 1.02 (-0.87; 2.91) | 0.29 | -0.42 (-1.70; 0.85) | 0.51 |
| S' tricuspid | 0.003 (-0.53; 0.54) | 0.99 | 0.02 (-1.02; 1.06) | 0.97 | -0.13 (-1.49; 1.23) | 0.85 | -0.27 (-1.05; 0.51) | 0.50 |

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|--------------------|---|--------------------------|--------------------------|---------------------------------------|
| TR Gradient | -2.49 (-4.40; -0.49) 0.02 | -3.39 (-7.26; 0.48) 0.09 | -1.92 (-6.19; 2.36) 0.37 | -2.44 (-5.91; 1.04) 0.17 |
| PASP | -2.89 (-5.26; -0.52) 0.02 | -3.53 (-8.27; 1.20) 0.14 | -1.94 (-6.59; 2.72) 0.41 | -2.40 (-6.45; 1.66) 0.25 |
| GLS | 0.25 (-0.35; 0.85) 0.41 | 0.34 (-0.89; 1.57) 0.59 | -0.48 (-1.90; 0.93) 0.50 | 1.20 (0.39; 2.02) 0.004 |

Each regression coefficient, derived from multivariable linear regression analysis is adjusted for the baseline value of the variable and age. Sex is coded as male = 1 and females = 0 so that positive regression coefficient indicates that at 1 year, the mean value of the relevant variable was higher in males than in females. Negative regression coefficient indicates that at 1 year, the mean value of the relevant variable was higher in females than in males. BSA – body surface area, E/A – mitral inflow E/A ratio, EF – ejection fraction, GLS – global longitudinal strain, IVSd – interventricular systolic wall thickness in diastole, LAD – left atrial diameter, LAA – left atrial area, LVEDD – left ventricular end diastolic diameter, LVEDV – left ventricular end diastolic volume, LVESD – left ventricular end systolic diameter, LVESV – left ventricular end systolic volume, MAPSE – mitral annular plane systolic excursion, MR – mitral regurgitation, MWT – mean wall thickness, PASP – pulmonary artery systolic pressure, PWTd – posterior wall thickness in diastole, RAA – right atrial area, RV S' velocity – right ventricle systolic excursion velocity, SV – stroke volume, TAPSE – tricuspid annular plane systolic excursion, TAPSE/PASP – tricuspid annular plane systolic excursion to pulmonary artery systolic pressure ratio, TR – tricuspid regurgitation

Supplementary Table 4 – Hazard ratio (HR) with 95% confidence interval (CI) comparing the hazard of death in males and females

| | All patients (n=906; 116 females) | | Wild-type (n=595; 26 females) | | T60A (n=99; 29 females) | | V122I (n=212; 61 females) | |
|--|-----------------------------------|----------------|-------------------------------|----------------|-------------------------|----------------|---------------------------|----------------|
| Echocardiographic variable as covariate | HR (95% CI) | P-value | HR (95% CI) | P-value | HR (95% CI) | P-value | HR (95% CI) | P-value |
| IVSd index to BSA | 0.91 (0.70-1.17) | 0.45 | 1.10 (0.64-1.87) | 0.74 | 0.68 (0.39-1.18) | 0.17 | 0.91 (0.70-1.67) | 0.45 |
| RWT | 0.90 (0.70-1.16) | 0.41 | 1.10 (0.64-1.87) | 0.74 | 0.66 (0.38-1.14) | 0.14 | 0.90 (0.70-1.16) | 0.41 |
| SV index to BSA | 0.98 (0.75-1.27) | 0.87 | 1.11 (0.65-1.90) | 0.70 | 0.81 (0.44-1.48) | 0.49 | 0.98 (0.75-1.27) | 0.87 |
| EF (%) | 0.93 (0.72-1.20) | 0.57 | 1.08 (0.63-1.85) | 0.78 | 0.69 (0.39-1.22) | 0.20 | 0.93 (0.72-1.20) | 0.57 |
| LAA 4ch index to BSA | 0.94 (0.72-1.21) | 0.62 | 1.11 (0.65-1.89) | 0.71 | 0.59 (0.32-1.08) | 0.09 | 0.94 (0.72-1.21) | 0.62 |
| RAA 4ch index to BSA | 0.87 (0.67-1.12) | 0.29 | 1.04 (0.61-1.78) | 0.88 | 0.68 (0.38-1.22) | 0.19 | 0.87 (0.67-1.13) | 0.29 |
| E/A Ratio | 0.96 (0.68-1.35) | 0.81 | 1.24 (0.58-2.67) | 0.58 | 0.79 (0.40-1.56) | 0.49 | 0.96 (0.68-1.35) | 0.81 |
| E/e' average | 1.05 (0.79-1.40) | 0.71 | 1.29 (0.71-2.35) | 0.41 | 0.69 (0.35-1.37) | 0.29 | 1.05 (0.79-1.40) | 0.71 |
| MAPSE | 0.93 (0.71-1.22) | 0.61 | 1.10 (0.65-1.89) | 0.72 | 0.71 (0.40-1.28) | 0.26 | 0.93 (0.71-1.22) | 0.61 |
| TAPSE | 0.93 (0.72-1.22) | 0.61 | 1.10 (0.64-1.88) | 0.73 | 0.69 (0.39-1.23) | 0.21 | 0.93 (0.72-1.22) | 0.61 |
| MR change – absolute | 0.92 (0.71-1.18) | 0.51 | 1.11 (0.65-1.89) | 0.71 | 0.61 (0.34-1.11) | 0.10 | 0.92 (0.71-1.18) | 0.51 |

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|--|-----------------------|-----------------------|-----------------------|-----------------------|
| MR change by ≥ 2 grades | 0.92 (0.71-1.18) 0.51 | 1.05 (0.62-1.80) 0.85 | 0.66 (0.37-1.15) 0.14 | 0.92 (0.71-1.18) 0.51 |
| AR change – absolute | 0.92 (0.71-1.19) 0.54 | 1.10 (0.65-1.89) 0.72 | 0.67 (0.38-1.17) 0.16 | 0.92 (0.71-1.19) 0.54 |
| AR change by ≥ 1 grade | 0.92 (0.72-1.19) 0.54 | 1.11 (0.65-1.89) 0.71 | 0.68 (0.39-1.19) 0.17 | 0.92 (0.72-1.19) 0.54 |
| AR change by ≥ 2 grades | 0.93 (0.72-1.19) 0.55 | 1.11 (0.65-1.91) 0.70 | 0.68 (0.39-1.21) 0.19 | 0.93 (0.72-1.19) 0.55 |
| TR change – absolute | 0.92 (0.72-1.19) 0.54 | 1.10 (0.65-1.89) 0.72 | 0.62 (0.36-1.10) 0.10 | 0.92 (0.72-1.19) 0.54 |
| TR change by ≥ 1 grade | 0.92 (0.72-1.19) 0.54 | 1.10 (0.64-1.88) 0.73 | 0.68 (0.39-1.20) 0.18 | 0.92 (0.72-1.19) 0.54 |
| PASP | 1.04 (0.77-1.40) 0.82 | 0.97 (0.54-1.74) 0.91 | 0.69 (0.33-1.44) 0.32 | 1.04 (0.77-1.40) 0.82 |
| GLS | 0.91 (0.70-1.19) 0.50 | 1.12 (0.64-1.95) 0.70 | 0.67 (0.37-1.21) 0.18 | 0.91 (0.70-1.19) 0.50 |

Each hazard ratio derived from a multivariable cox proportional hazards regression analysis which adjusts for the change in the relevant echocardiographic variable from baseline to 1 year. Sex coded as male = 1 and female = 0 such that a Hazard Ratio of 1.10 indicates that the hazard of death is 1.10 times greater in males compared to female. AR – aortic regurgitation, BSA – body surface area, E/A – mitral inflow E:A ratio, EF – ejection fraction, GLS – global longitudinal strain, IVSd – interventricular systolic wall thickness in diastole, LAA – left atrial area, MAPSE – mitral annular plane systolic excursion, MR – mitral regurgitation, PASP – pulmonary artery systolic pressure, RAA – right atrial

area, RV S' velocity – right ventricle systolic excursion velocity, RWT – relative wall thickness, SV – stroke volume, TAPSE – tricuspid annular plane systolic excursion.

Supplementary table A – Multivariable linear regression analysis of interventricular septum in diastole (IVSd) indexed to height

| Comparison | Regression coefficient | SE | P value |
|--------------------------------------|------------------------|--------|---------|
| Sex (males vs female*) | 0.3339 | 0.1099 | 0.002 |
| Genotype (wild-type vs V122I) | 0.0228 | 0.0881 | 0.796 |
| Genotype (T60A vs wild-type*) | 0.2500 | 0.1193 | 0.036 |
| Genotype (T60A vs V122I*) | 0.2728 | 0.1290 | 0.035 |

The regression coefficient represents the estimated difference in means between the two groups. Sex and genotype are coded such that a coefficient >0 indicates that the mean IVSd indexed to height was higher in the second variable compared to the first variable and when adjusted for other variables in the model. *Significant comparator. BSA – body surface area, IVSd – interventricular septum in diastole. SE – standard error

Supplementary table B – Multivariable linear regression analysis of interventricular septum in diastole (IVSd) indexed to body surface area (BSA)

| Comparison | Regression coefficient | SE | P value |
|--------------------------------------|------------------------|--------|---------|
| Sex (male vs female*) | 0.7712 | 0.1237 | <0.001 |
| Genotype (wild-type vs V122I) | 0.0751 | 0.9917 | 0.449 |
| Genotype (T60A vs V122I) | 0.0130 | 0.1452 | 0.929 |
| Genotype (T60A vs wild-type) | 0.0621 | 0.1346 | 0.644 |

The regression coefficient represents the estimated difference in means between the two groups. Sex and genotype are coded such that a positive coefficient >0 indicates that the mean IVSd indexed to BSA was higher in the second variable compared to the first variable and when adjusted for other variables in the model. *Significant comparator. BSA – body surface area, IVSd – interventricular septum in diastole, SE – standard error

Supplementary Figure 1 – Proportion of males and females within tertiles of both non-indexed and indexed interventricular septum in diastole (IVSd)

