Patients with p.(T80A) hATTR-cardiac amyloidosis diagnosed between 2002-2021 (n=212)

| Variables                                    | 2002 – 2006 (n=24) | 2007 – 2011 (n=41) | 2012 – 2016 (n=64) | 2017 – 2021 (n=83) | P-value |
|----------------------------------------------|--------------------|--------------------|--------------------|--------------------|---------|
| **Baseline Characteristics**                 |                    |                    |                    |                    |         |
| Age                                          | 64.42 ± 4.30       | 67.88 ± 5.23       | 67.08 ± 7.05       | 65.46 ± 6.91       | 0.006   |
| Sex (male)                                   | 19 (79.2%)         | 27 (65.9%)         | 45 (70.3%)         | 60 (72.3%)         | 0.708   |
| BSA                                          | -                  | 1.75 ± 0.21        | 2.14 ± 2.45        | 1.85 ± 0.24        | 0.292   |
| Duration of symptoms before diagnosis (months)| 48 (24-57) by r    | 24 (12-48) by c    | 12 (3-24)          | 9 (2-23)           | <0.001  |
| NYHA class                                   |                    |                    |                    |                    | <0.001  |
| 1                                           | 0 (0.0%)           | 8 (19.5%)          | 12 (18.8%)         | 27 (32.5%)         |         |
| 2                                           | 6 (25.0%)          | 17 (41.5%)         | 41 (64.1%)         | 47 (56.6%)         |         |
| 3                                           | 4 (16.7%)          | 9 (22.0%)          | 9 (14.1%)          | 7 (8.4%)           |         |
| 4                                           | 3 (12.5%) by r     | 2 (4.9%)           | 1 (1.6%)           | 0 (0.0%)           |         |
| Missing                                      | 11 (45.8%)         | 5 (12.2%)          | 1 (1.6%)           | 2 (9.6%)           |         |
| **NAC stage**                                |                    |                    |                    |                    | 0.009   |
| 1                                           | 9 (37.5%) γ        | 21 (51.2%) ε       | 41 (64.1%)         | 61 (73.5%)         |         |
| 2                                           | 7 (29.2%)          | 17 (41.5%)         | 18 (28.1%)         | 12 (14.5%)         |         |
| 3                                           | 3 (12.5%)          | 2 (4.9%)           | 4 (6.3%)           | 2 (2.4%)           |         |
| Missing                                      | 5 (20.8%)          | 1 (2.4%)           | 1 (1.6%)           | 8 (2.4%)           |         |
| 6-minute walk test (meters)                  | -                  | -                  | 357 (247-426) φ    | 448 (366-529)      | <0.001  |
| 6-minute walk test (% predicted)             | -                  | -                  | 62.80 ± 24.21 φ    | 81.78 ± 20.38      | <0.001  |
| NT-pro-BNP (pg/L)                            | 3324 (1146-11050) γ| 1945 (1311-4956) ε | 2106 (930-4313)    | 1187 (618-2526)    | 0.003   |
| eGFR (ml/min/1.73m²)                         | 74 (57-87)         | 79 (63-90)         | 86 (62-90)         | 77 (65-89)         | 0.048   |
| **Echocardiographic variables**              |                    |                    |                    |                    |         |
| IVSd (mm)                                    | 18.53 ± 4.64       | 17.23 ± 3.05       | 16.81 ± 2.44       | 16.17 ± 2.68       | 0.034   |
| IVSd indexed (mm/m²)                         | -                  | 9.97 ± 2.17        | 9.29 ± 1.71        | 8.89 ± 1.58        | 0.041   |
| PWTd (mm)                                    | 17.80 ± 4.31       | 16.70 ± 2.78       | 16.67 ± 2.55       | 15.59 ± 2.87       | 0.027   |
| PWTd indexed (mm/m²)                         | -                  | 9.65 ± 1.83        | 9.21 ± 1.72        | 8.55 ± 1.69        | 0.008   |
| LV mass (g)                                  | 355.01 ± 120.09    | 296.63 ± 69.36     | 325.25 ± 91.60     | 284.11 ± 94.58     | 0.009   |
| LV mass indexed (g/m³)                       | -                  | 170.30 ± 37.64     | 177.97 ± 48.51     | 153.67 ± 46.26     | 0.020   |
| LVEDV (ml)                                   | -                  | 70.58 ± 25.26      | 72.39 ± 22.24      | 83.97 ± 31.77      | 0.008   |
| LVEDV indexed (ml/m³)                        | -                  | 40.41 ± 13.10      | 38.72 ± 11.47      | 40.73 ± 19.15      | 0.041   |
| LVESV (ml)                                   | -                  | 35.53 ± 15.21      | 36.19 ± 15.41      | 40.44 ± 19.18      | 0.186   |
| LVESV indexed (ml/m²)                        | -                  | 20.45 ± 8.43       | 19.36 ± 7.89       | 21.61 ± 9.97       | 0.231   |
| SV (ml)                                      | -                  | 35.06 ± 14.89 ε    | 36.21 ± 10.67      | 43.50 ± 17.83      | 0.009   |
| SV indexed (ml/m²)                           | -                  | 19.96 ± 7.88       | 19.36 ± 5.74       | 23.09 ± 8.83       | 0.026   |
| EF (%)                                       | -                  | 49.74 ± 10.14      | 50.91 ± 9.17       | 52.07 ± 10.41      | 0.498   |
| LS (%)                                       | -                  | -10.68 ± 4.17 δ    | -12.10 ± 3.28      | -12.08 ± 4.14      | 0.036   |
| MAPSE (mm)                                   | -                  | 8.17 ± 2.47        | 8.06 ± 2.42        | 8.81 ± 2.77        | 0.291   |
| TAPSE (mm)                                   | -                  | 15.60 ± 4.75       | 16.34 ± 4.28       | 17.12 ± 4.76       | 0.196   |
| E/A                                          | -                  | 1.68 ± 0.97        | 1.52 ± 0.83        | 1.62 ± 1.00        | 0.931   |
| E/e’ average                                 | -                  | 19.17 ± 8.01       | 18.76 ± 8.09       | 17.33 ± 7.73       | 0.470   |
| LAA (cm²)                                    | -                  | 23.35 ± 4.66       | 24.31 ± 5.02       | 22.18 ± 4.95       | 0.096   |
| LAA indexed (cm²/m²)                         | -                  | 13.36 ± 2.63       | 13.24 ± 3.27       | 12.09 ± 2.60       | 0.025   |
| RAA (cm²)                                    | -                  | 20.43 ± 5.99       | 20.81 ± 5.03       | 19.10 ± 5.09       | 0.325   |
| RAA indexed (cm²/m²)                         | -                  | 11.55 ± 2.88       | 11.18 ± 2.67       | 10.36 ± 2.40       | 0.087   |
| Significant MR                              | 0 (0.0%)           | 3 (7.3%)           | 7 (10.9%)          | 2 (2.4%)           | 0.085   |
| Significant TR                              | 0 (0.0%)           | 5 (12.2%)          | 8 (12.5%)          | 4 (4.8%)           | 0.114   |
**Supplementary Table S4.** Baseline characteristics and echocardiographic parameters for patients with p.(T80A) hATTR cardiac amyloidosis separated by the year of diagnosis.

P-values for pairwise comparison: $\alpha = P<0.01$ for 2002-2006 vs. 2007-2011, $\beta = P<0.01$ for 2002-2006 vs. 2012-2016, $\gamma = P<0.01$ for 2002-2006 vs. 2017-2021, $\delta = P<0.01$ for 2007-2011 vs. 2012-2016, $\epsilon = P<0.01$ for 2007-2011 vs. 2017-2021, $\phi = P<0.01$ for 2012-2016 vs. 2017-2021

BSA = Body surface area; NYHA = New York Heart Association; NAC = National Amyloidosis Centre; NT-pro-BNP = N-terminal pro B-type natriuretic peptide; eGFR = Estimated glomerular filtration rate; IVSd = Interventricular septum in diastole; PWTd = Posterior wall thickness in diastole; LVEDV = Left ventricular end diastolic volume; LVEDV = Left ventricular end systolic volume; SV = Stroke volume; EF = Ejection fraction; LS = Longitudinal strain; MAPSE = Mitral annular plane systolic excursion; TAPSE = Tricuspid annular plane systolic excursion; LAA = Left atrial area (measured in the 4-chamber view); RAA = Right atrial area (measured in the 4 chamber view); MR = Mitral regurgitation; TR = Tricuspid regurgitation; AS = Aortic stenosis; PASP = Pulmonary artery systolic pressure.

| Significant AS | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 1 (1.2%) | 0.668 |
|----------------|---------|---------|---------|---------|-------|
| PASP (mmHg)    | 48.80 ± 6.91 | 37.13 ± 13.37 | 36.51 ± 10.33 | 28.90 ± 15.95 | <0.001 |
| TAPSE/PASP     | -       | 0.45 ± 2.46 | 0.52 ± 0.41 | 0.84 ± 0.89 | 0.021 |