**Online Supplementary Data**

Distinctive deposition patterns of sporadic transthyretin-derived amyloidosis in the atria: A forensic autopsy-based study

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**List of Supplementary material**

Supplementary Table: 3

**Supplementary Table 1.** Summary of semi-quantitative histopathological investigation results

|  |  |  |  |
| --- | --- | --- | --- |
|  | Transthyretin |  | Atrial natriuretic factor |
|  | VS | AS | RA | RAA | LA | LAA | SVC | SAN | AVN | Neu\* | GC |  | AS | RAA | RA | LAA | LA | SVC |
| # | E | V | I | ER | EL | V | I | E | V | I | E | V | I | E | V | I | E | V | I | E | V | I |  |
| 1 | 0 | 0 | 1 | 0 | 0 | 0 | 1 | 1 | 0 | 1 | 1 | 0 | 1 | 1 | 1 | 1 | 1 | 0 | 1 | 0 | 0 | 1 | Neg | Neg | Neg | Neg |  | 0 | 3 | 2 | 3 | 2 | 0 |
| 2 | 0 | 0 | 3 | 4 | 1 | 1 | 4 | 3 | 2 | 1 | 2 | 0 | 1 | 2 | 1 | 3 | 1 | 1 | 4 | 2 | 0 | 3 | Neg | Neg | Neg | Neg |  | 2 | 2 | 2 | 3 | 2 | 1 |
| 3 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 1 | 0 | 0 | 1 | Neg | Neg | Neg | Neg |  | 2 | 2 | 1 | 3 | 2 | 0 |
| 4 | 0 | 0 | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 1 | 0 | 0 | 1 | 0 | 0 | 1 | 0 | 0 | 0 | Neg | Neg | Neg | Neg |  | 2 | 1 | 2 | 2 | 2 | 0 |
| 5 | 0 | 1 | 3 | 2 | 3 | 0 | 3 | 1 | 0 | 2 | 2 | 1 | 2 | 2 | 1 | 3 | 1 | 0 | 2 | 2 | 0 | 1 | Pos | Neg | Neg | Neg |  | 3 | 2 | 2 | 4 | 3 | 0 |
| 6 | 0 | 2 | 3 | 4 | 1 | 2 | 2 | 1 | 2 | 1 | 1 | 4 | 1 | 2 | 4 | 3 | 1 | 2 | 2 | 3 | 1 | 3 | Neg | Neg | Pos | Neg |  | 2 | 3 | 2 | 2 | 2 | 1 |
| 7 | 0 | 0 | 3 | 2 | 0 | 0 | 2 | 2 | 1 | 1 | 1 | 0 | 1 | 1 | 1 | 2 | 1 | 1 | 2 | 3 | 0 | 1 | Neg | Neg | Neg | Neg |  | 3 | 3 | 3 | 3 | 4 | 2 |
| 8 | 1 | 1 | 3 | 3 | 0 | 1 | 3 | 0 | 0 | 0 | 0 | 0 | 0 | 3 | 1 | 4 | 4 | 1 | 3 | 0 | 0 | 1 | Neg | Neg | Equ | Pos |  | 1 | 2 | 1 | 2 | 1 | 1 |
| 9 | 0 | 0 | 1 | 1 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 1 | 1 | 0 | 1 | Neg | Neg | Neg | Neg |  | 1 | 2 | 1 | 3 | 2 | 1 |
| 10 | 1 | 3 | 4 | 4 | 3 | 1 | 4 | 3 | 3 | 4 | 3 | 4 | 2 | 3 | 3 | 4 | 3 | 3 | 3 | 4 | 2 | 3 | Pos | Neg | Equ | Neg |  | 4 | 2 | 2 | 3 | 2 | 1 |
| 11 | 0 | 1 | 2 | 1 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 2 | 1 | 4 | 0 | 0 | 1 | 1 | 0 | 1 | Neg | Neg | Equ | Neg |  | 0 | 0 | 0 | 1 | 0 | 0 |
| 12 | 1 | 2 | 4 | 4 | 1 | 1 | 4 | 1 | 1 | 1 | 1 | 1 | 1 | 2 | 1 | 4 | 2 | 1 | 2 | 4 | 0 | 2 | Neg | Neg | Neg | Neg |  | 1 | 2 | 2 | 2 | 2 | 0 |
| 13 | 0 | 3 | 0 | 4 | 0 | 1 | 4 | 0 | 1 | 0 | 0 | 2 | 0 | 2 | 2 | 2 | 1 | 3 | 4 | 4 | 2 | 4 | Neg | Neg | Neg | Pos |  | 0 | 2 | 1 | 3 | 3 | 1 |
| 14 | 0 | 4 | 1 | 0 | 0 | 3 | 0 | 0 | 3 | 0 | 0 | 3 | 0 | 2 | 3 | 1 | 0 | 4 | 1 | 0 | 3 | 0 | Neg | Neg | Neg | Neg |  | 2 | 1 | 1 | 2 | 3 | 1 |
| 15 | 0 | 0 | 2 | 4 | 0 | 0 | 2 | 1 | 2 | 1 | 4 | 1 | 1 | 1 | 1 | 2 | 0 | 0 | 2 | 3 | 0 | 1 | Neg | Neg | Neg | Neg |  | 1 | 1 | 0 | 1 | 1 | 0 |
| 16 | 0 | 0 | 3 | 4 | 0 | 0 | 3 | 3 | 1 | 2 | 2 | 0 | 0 | 3 | 1 | 4 | 4 | 0 | 3 | 2 | 0 | 2 | Neg | Neg | Neg | Neg |  | 1 | 1 | 1 | 1 | 1 | 1 |
| 17 | 0 | 3 | 4 | 4 | 1 | 2 | 4 | 2 | 2 | 1 | 2 | 1 | 2 | 3 | 3 | 4 | 2 | 2 | 2 | 3 | 1 | 2 | Neg | Neg | Equ | Neg |  | 2 | 2 | 1 | 2 | 1 | 1 |
| 18 | 0 | 1 | 2 | 1 | 0 | 0 | 1 | 0 | 2 | 1 | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 0 | 2 | 2 | 0 | 1 | Neg | Neg | Neg | Neg |  | 2 | 2 | 2 | 2 | 2 | 1 |
| 19 | 2 | 0 | 4 | 2 | 1 | 1 | 4 | 4 | 3 | 4 | 1 | 1 | 2 | 2 | 3 | 4 | 1 | 1 | 2 | 4 | 2 | 4 | Pos | Neg | Pos | Neg |  | 1 | 1 | 1 | 1 | 2 | 1 |
| 20 | 0 | 0 | 1 | 3 | 0 | 1 | 1 | 0 | 0 | 0 | 1 | 0 | 1 | 1 | 1 | 1 | 0 | 0 | 1 | 0 | 0 | 1 | Neg | Neg | Neg | Neg |  | 1 | 3 | 1 | 1 | 1 | 1 |

**Abbreviations:** AS, atrial septum; AVN, atrioventricular septum; E, endocardium; EL, endocardium in the left side; Equ, equivocal; ER, endocardium in the right side; I, interstitium; IHC, immunohistochemistry; LA, left atrium; LAA, left atrial appendage; Neg, negative; N/P, neural/perineural involvement; pCR, phenol Congo red; Pos, positive; RA, right atrium; RAA, right atrial appendage; SVC, superior vena cava; V, vessel

\* Positive means positive deposition in the nerve; equivocal means positive deposition in the perineurium but negative deposition in the nerve.

**Supplementary Table 2.** Summary of the quantitative analysis results of ATTR deposition burden

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| Case # | VS | AS | RA | RAA | LA | LAA | SVC |
| 1 | 0.515 | 0.067 | 0.209 | 0.03 | 0.832 | 0.291 | 0.682 |
| 2 | 10.488 | 15.214 | 0.821 | 0.459 | 10.866 | 18.486 | 10.561 |
| 3 | 1.011 | 0 | 0.114 | 0 | 0.601 | 0.017 | 0.023 |
| 4 | 5.33 | 0 | 0.572 | 0.038 | 0.304 | 1.175 | 0 |
| 5 | 15.768 | 12.275 | 3.917 | 3.383 | 9.758 | 6.139 | 0.776 |
| 6 | 9.643 | 4.879 | 0.657 | 0.148 | 8.986 | 5.588 | 7.159 |
| 7 | 9.16 | 2.374 | 0.723 | 0.243 | 1.728 | 3.425 | 1.473 |
| 8 | 13.323 | 14.949 | 0 | 0 | 14.506 | 12.534 | 1.179 |
| 9 | 0.126 | 0.174 | 0 | 0 | 0.574 | 0.104 | 0.104 |
| 10 | 23.985 | 17.264 | 15.247 | 3.998 | 3 | 13.228 | 12.045 |
| 11 | 2.029 | 0.808 | 0 | 0 | 13.752 | 0.579 | 0.005 |
| 12 | 24.87 | 23.509 | 0.354 | 1.09 | 18.431 | 7.355 | 4.396 |
| 13 | 0 | 20.828 | 0 | 0 | 7.077 | 16.469 | 18.695 |
| 14 | 0.025 | 0 | 0 | 0 | 0.143 | 0.095 | 0 |
| 15 | 2.264 | 6.059 | 0.388 | 0.66 | 1.669 | 1.758 | 0.46 |
| 16 | 8.711 | 7.135 | 6.685 | 0 | 18.308 | 14.014 | 6.015 |
| 17 | 17.164 | 16.947 | 0.62 | 6.149 | 13.969 | 4.658 | 5.774 |
| 18 | 5.346 | 1.024 | 0.155 | 0 | 1.439 | 3.595 | 0.128 |
| 18 | 24.166 | 19.217 | 19.897 | 7.109 | 16.785 | 7.123 | 16.983 |
| 20 | 0.031 | 0.18 | 0 | 0.134 | 0.054 | 0.074 | 0.077 |
| Mean | 8.7 | 8.1 | 1.2 | 2.5 | 5.8 | 7.1 | 4.3 |
| SD | 8.4 | 8.2 | 2.1 | 5.3 | 5.9 | 6.7 | 5.8 |
| Min | 0 | 0 | 0 | 0 | 0.05 | 0.02 | 0 |
| Max | 24.9 | 23.5 | 7.1 | 19.9 | 18.5 | 18.4 | 18.7 |

**Abbreviation:** SD, standard deviation

**Supplementary Table 3.** Summary of comparison of semiquantitative analysis results in right and left atria and atrial appendages.

|  |
| --- |
| Semiquantitative ATTR deposition grading (range) |
| Region | Right | Left | *P* value\* |
| Atrial septum | Endocardium | 2.4 ± 1.6 (0–4) | 0.6 ± 0.9 (0–3) | **<0.01** |
| Atrium | Endocardium | 1.1 ± 1.3 (0–4) | 1.7 ± 1.0 (0–3) | 0.88 |
| Vessel | 1.2 ± 1.1 (0–3) | 1.5 ± 1.1 (0–4) | 0.80 |
| Interstitium | 1.1 ± 1.1 (0–4) | 2.5 ± 1.3 (1–4) | **<0.01** |
| Atrial appendage | Endocardium | 1.1 ± 1.1 (0–4) | 1.2 ± 1.2 (0–4) | 0.10 |
| Vessel | 0.9 ± 1.3 (0–4) | 1.0 ± 1.2 (0–4) | 0.41 |
| Interstitium | 0.8 ± 0.7 (0–2) | 2.0 ± 0.9 (1–4) | **<0.01** |
| Semiquantitative AANF deposition grading (range) |
| Region | Right | Left | *P* value |
| Atrium | Interstitium | 1.4 ± 0.7 (0–3) | 1.9 ± 0.9 (0–4) | 0.28 |
| Atrial appendage | Interstitium | 1.9 ± 0.8 (0–3) | 2.2 ± 0.8 (1–4) | 0.10 |
| Quantitative ATTR deposition burden (%) |
| Region | Right | Left | *P* value |
| Atrium | Interstitium | 2.5 ± 5.3 (0–19.9) | 7.7 ± 6.8 (0.1–18.4) | **<0.01** |
| Atrial appendage | Interstitium | 1.2 ± 2.1 (0–7.1) | 5.8 ± 5.9 (0–18.5) | **<0.01** |

**Boldface** signifies values that are statistically significant at *p* < 0.05.

\* Right vs. Left, compared using the Mann-Whiteny U test.