Title: Neuropathologic Scales of Cerebrovascular Disease Associated with Diffusion Changes on MRI

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Table S1. Antibodies used in immunohistochemical staining.

| Antibody Name                        | Clone                          | Concentration | Host | Source          | Catalog #   |
|--------------------------------------|--------------------------------|---------------|------|-----------------|-------------|
| Anti-Beta-amyloid                    | Monoclonal (6F/3D)             | 1:100         | Mouse | DAKO            | M0872       |
| Anti-phosphoPHF-tau                  | Monoclonal (AT8)               | 1:100         | Mouse | ThermoFisher    | MN1020      |
| Anti-phosphoTDP-43                   | Monoclonal (pS409/410)         | 1:10,000      | Mouse | Cosmo Bio       | TIP-PTD-M01 |
| Anti-Myelin Basic Protein            | Monoclonal (119-131, clone 2)  | 1:500         | Mouse | Millipore/Sigma | MAB381      |
| Anti-Neurofilament, Phosphorylated   | Monoclonal (SMI-31)            | 1:40,000      | Mouse | Covance         | SMI-31R     |
Table S2. Modified Kalaria CVD Score Rubric

| Cerebrovascular disease scale [5-6] |  |
|------------------------------------|---|
| **Cerebral Cortex** (select highest that applies) |  |
| □ 0 Normal appearance of brain, vessels, white matter, and cortex |  |
| □ 1 Mild modification of vessel walls, perivascular spaces, or white matter |  |
| □ 2 Moderate to severe but isolated modification of the vessel (arteriolosclerosis or amyloid angiopathy), usually associated with hemosiderin deposits in the perivascular spaces; and/or Moderate to severe cerebral amyloid angiopathy involving parenchyma |  |
| □ 3 Moderate to severe perivascular space dilatations either in the deep or the juxtacortical white matter |  |
| □ 4 Moderate to severe myelin loss; and/or White matter infarct |  |
| □ 5 Presence of cortical microinfarcts |  |
| □ 6 Presence of large infarcts and/or cystic infarcts |  |
| **Basal ganglia** (select highest that applies) |  |
| □ 0 Normal appearance |  |
| □ 1 Mild modification of vessel walls or perivascular spaces (or if PVS not noted, but isolated moderate to severe arteriolosclerosis) |  |
| □ 2 Moderate to severe perivascular space dilatations |  |
| □ 3 Presence of microinfarcts |  |
| □ 4 Presence of large infarcts; and/or lacunar infarct |  |
| **Kalaria score** (Total of cortex and basal ganglia) | (out of 10) |
| Strozyk Scale Rubric |  |
|----------------------|--|
| **Large infarct**    |  |
| None                 | 0 |
| 1 large infarct      | 1 |
| >2 large infarcts    | 2 |
| **Lacunar/Cystic infarcts** |  |
| None                 | 0 |
| 1 lacunar infarct    | 1 |
| >2 large infarcts    | 2 |
| **Leukoencephalopathy** |  |
| None                 | 0 |
| Mild                 | 1 |
| Moderate-to-Severe   | 2 |
| **Total vascular score** | (out of 6) |

Table S4. Neuropathologic Characteristics of cases

| Case Number | Sex  | PMI (hours) | Braak Stage | Thal Phase | Neuropathologic Diagnosis(es) | Kalaria Score | Strozyk Score | APOE ε4 |
|-------------|------|-------------|-------------|------------|------------------------------|---------------|---------------|---------|
| 1           | Male | 19          | IV          | 3          | Intermediate ADNC           | 3             | 0             | No      |
| 2           | Male | 11          | II          | 4          | Low ADNC                    | 2             | 1             | Yes     |
| 3           | Male | 14          | III         | 3          | Intermediate ADNC           | 3             | 1             | No      |
| 4           | Female | 18        | IV          | 5          | Intermediate ADNC           | 5             | 2             | Yes     |
| 5           | Female | 18        | IV          | 1          | No ADNC                     | 6             | 1             | No      |
| 6           | Male | 6           | IV          | 2          | No ADNC                     | 3             | 1             | No      |
| 7           | Male | 7           | IV          | 5          | Intermediate ADNC           | 6             | 1             | No      |
| 8           | Male | 19          | I           | 2          | Low ADNC                    | 6             | 2             | No      |
| 9           | Female | 21        | III         | 0          | No ADNC                     | 2             | 0             | No      |
| 10          | Female | 3        | V           | 5          | High ADNC                   | 3             | 0             | No      |
| 11          | Male | 12          | V           | 5          | High ADNC                   | 3             | 1             | Yes     |
| 12          | Male | 4           | III         | 3          | Intermediate ADNC           | 3             | 1             | No      |
| 13          | Male | 21          | II          | 1          | Low ADNC                    | 6             | 0             | Yes     |
| 14          | Female | 30        | IV          | 2          | Low ADNC                    | 7             | 1             | Yes     |
| 15          | Male | 23          | III         | 0          | No ADNC                     | 7             | 2             | No      |
| 16          | Female | 44        | II          | 5          | Low ADNC                    | 2             | 0             | Yes     |
| 17          | Male | 16          | III         | 3          | Intermediate ADNC           | 2             | 0             | No      |
| 18          | Male | 7           | IV          | 3          | Intermediate ADNC           | 7             | 3             | Yes     |
| 19          | Male | 21          | II          | 1          | Low ADNC                    | 3             | 1             | No      |
| 20          | Female | 46        | II          | 4          | Low ADNC                    | 7             | 4             | Yes     |
| 21          | Male | 18          | III         | 1          | No ADNC                     | 2             | 0             | No      |
| 22          | Female | 19        | III         | 0          | No ADNC                     | 2             | 0             | Yes     |
| 23          | Male | 11          | III         | 5          | Intermediate ADNC, Transitional LBD | 3             | 1             | Yes     |
| 24          | Female | 51        | II          | 3          | Low ADNC                    | 3             | 1             | No      |
| 25          | Male | 5           | VI          | 5          | High ADNC, Amygdala-predominant Lewy bodies | 8             | 4             | No      |
| 26          | Male | 5           | III         | 2          | No ADNC                     | 0             | 2             | No      |
| 27          | Female | 14        | I           | 3          | No ADNC                     | 2             | 0             | Yes     |
| 28          | Female | 21        | III         | 3          | No ADNC                     | 3             | 1             | No      |
| 29          | Male | 12          | III         | 0          | No ADNC                     | 3             | 1             | No      |
| 30          | Male | 13          | V           | 3          | Intermediate ADNC, Amygdala-predominant Lewy bodies | 3             | 3             | No      |
| 31          | Male | 16          | II          | 5          | Low ADNC, Transitional LBD  | 6             | 1             | Yes     |
| 32          | Male | 27          | II          | 1          | No ADNC                     | 2             | 0             | No      |
| 33          | Male | 9           | V           | 4          | High ADNC                   | 3             | 1             | Yes     |
| 34          | Female | 15        | III         | 0          | No ADNC                     | 10            | 4             | No      |
|   | Gender | Age | Stage | ADNC | Brainstem LBD | PMI | Score | Postmortem | ADNC | Result |
|---|--------|-----|-------|------|---------------|-----|-------|-------------|------|--------|
| 35 | Male   | 21  | III   | 1    | No ADNC, Transitional LBD | 2   | 0     | No          |      |        |
| 36 | Male   | 4   | IV    | 0    | No ADNC, Transitional LBD | 7   | 2     | No          |      |        |
| 37 | Male   | 24  | IV    | 5    | Intermediate ADNC       | 3   | 1     | No          |      |        |
| 38 | Female | 46  | II    | 2    | Low ADNC                 | 3   | 1     | No          |      |        |
| 39 | Male   | 22  | III   | 1    | No ADNC, Brainstem LBD   | 2   | 0     | Yes         |      |        |
| 40 | Female | 45  | VI    | 5    | High ADNC, Diffuse LBD  | 3   | 3     | No          |      |        |
| 41 | Male   | 15  | III   | 0    | No ADNC                  | 3   | 1     | No          |      |        |
| 42 | Male   | 20  | I     | 0    | No ADNC                  | 0   | 0     | No          |      |        |
| 43 | Male   | 20  | III   | 1    | No ADNC                  | 3   | 1     | No          |      |        |
| 44 | Female | 6   | III   | 3    | Intermediate ADNC, Brainstem LBD | 3 | 0 | No | |
| 45 | Male   | 18  | IV    | 1    | Low ADNC, Brainstem LBD  | 3   | 1     | No          |      |        |
| 46 | Female | 15  | V     | 5    | High ADNC                | 5   | 4     | No          |      |        |
| 47 | Female | 10  | V     | 5    | High ADNC, Diffuse LBD   | 3   | 1     | Yes         |      |        |
| 48 | Male   | 9   | I     | 0    | No ADNC                  | 3   | 1     | No          |      |        |
| 49 | Female | 44  | V     | 5    | High ADNC                | 9   | 3     | Yes         |      |        |
| 50 | Male   | 13  | I     | 0    | No ADNC                  | 3   | 2     | No          |      |        |
| 51 | Female | 12  | III   | 1    | Intermediate ADNC, Brainstem LBD | 1 | 1 | No | |

**Abbreviations:** PMI, postmortem interval; ADNC, Alzheimer’s Disease Neuropathologic Change; LBD, Lewy Body Disease
Table S5. Characteristics table with the mean (SD) listed for the continuous variables and count (%) for the categorical variables.

|                          | Not Autopsied n = 843 | Autopsied n = 51 | P-value |
|--------------------------|------------------------|------------------|---------|
| Male, no. (%)            | 448 (53%)              | 32 (63%)         | 0.18    |
| Age, yrs                 | 84.7 (7.6)             | 83.8 (7.5)       | 0.41    |
| APOE ε4 carrier (%)      | 237 (29%)              | 16 (31%)         | 0.69    |
| Education, yrs           | 13.5 (2.9)             | 15.0 (3.2)       | <0.001  |
| Global                   | -1.39 (1.36)           | -0.98 (1.43)     | 0.064   |

P-values are from either a t-test or chi-squared test.
Table S6. Table of linear regression results with an adjustment for time from scan to death and weighted for time for the summary scores.

|                         | 5 years between scan and death (N=51) | 3 years between scan and death (N=31) |
|-------------------------|--------------------------------------|---------------------------------------|
|                         | Estimate (SE)  | P-value | R²   | Partial R² | Estimate (SE)  | P-value | R²   | Partial R² |
| Imaging Predicting Kalaria Scale |                      |         |     |            |                      |         |     |            |
| CVD Composite Score     | 0.07 (0.16)    | 0.67    | 0.0673 | 0.004      | 0.08 (0.21)    | 0.72    | 0.1174 | 0.005      |
| Modified Staals Score   | 0.04 (0.019)   | 0.066   | 0.1347 | 0.076      | 0.04 (0.023)   | 0.081   | 0.2124 | 0.112      |
| Imaging Predicting Strozyk Scale |                      |         |     |            |                      |         |     |            |
| CVD Composite Score     | -0.06 (0.09)   | 0.49    | 0.0449 | 0.011      | -0.04 (0.13)   | 0.75    | 0.0889 | 0.004      |
| Modified Staals Score   | 0.03 (0.01)    | 0.001   | 0.2431 | 0.216      | 0.04 (0.013)   | 0.006   | 0.3208 | 0.258      |
Figure S1. DTI parameter spaghetti plots, wherein serial lines are shown as a function of age.