**Supplementary Materials**

Table S1: Correlations between cardiovascular risk factors and IFs

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **CSVD markers** | **sex** | **age** | **BMI** | **Waist** | **HIP** | **Educa-tion** | **SBP** | **DBP** | **ALP** | **AST** | **GGT** | **CR** | **UA** | **FBG** | **PBG** | **HbA1c** |
| **WMH** | 0.26 (0.04, 1.36) | **1.14** **(1.03, 1.28) \*** | 1.08 (0.72, 1.61) | 0.98 (0.90, 1.13) | 1.08 (0.92, 1.21) | 0.89 (0.71, 1.11) | 1.01 (0.95, 1.07) | 0.97 (0.87, 1.07) | 0.99 (0.95, 1.02) | 1.09 (0.97, 1.30) | 1.08 (1.01, 1.20) | 1.00 (0.95, 1.07) | 1.00 (0.99, 1.01) | 2.45 (0.86, 8.46) | 0.94 (0.71, 1.28) | 1.58 (0.34, 10.14) |
| **Brain atrophy** | **3.95** **(2.38, 6.66) \*** | **1.47** **(1.41, 1.55) \*\*\*** | 1.08 (0.98, 1.20) | 0.95 (0.92, 0.98) | 0.97 (0.93, 1.01) | 1.04 (0.98, 1.11) | 0.97 (0.95, 0.98) | **1.09** **(1.06, 1.12) \*** | 0.99 (0.98, 1.00) | 0.98 (0.97, 1.00) | 1.01 (1.00, 1.03) | 1.00 (0.99, 1.01) | 1.00 (0.99, 1.00) | **1.94** **(1.47, 2.59) \*** | 1.00 (0.93, 1.06) | 1.00 (0.71, 1.42) |
| **EPVS** | 0.86 (0.43, 1.70) | **1.08** **(1.04, 1.12) \*\*\*** | 1.08 (0.93, 1.26) | 0.96 (0.92, 1.00) | 1.02 (0.96, 1.08) | 1.04 (0.96, 1.12) | 0.99 (0.97, 1.00) | 1.00 (0.97, 1.04) | 1.00 (0.99, 1.01) | 1.00 (0.97, 1.03) | 1.00 (0.99, 1.00) | 1.01 (0.99, 1.03) | 1.00 (1.00, 1.01) | 0.95 (0.70, 1.30) | 1.07 (0.99, 1.16) | 1.03 (0.64, 1.71) |
| **CMBs** | 1.07 (0.66, 1.73) | **1.05** **(1.03, 1.08) \*\*\*** | 0.97 (0.87, 1.08) | 0.99 (0.96, 1.03) | 0.98 (0.94, 1.02) | 1.01 (0.96, 1.07) | 1.00 (0.98, 1.01) | **1.03** **(1.01, 1.06) \*** | 1.00 (0.99, 1.01) | 1.01 (0.99, 1.03) | 1.00 (0.99, 1.00) | 1.00 (0.99, 1.02) | 1.00 (1.00, 1.00) | 0.92 (0.73, 1.16) | 1.02 (0.96, 1.08) | 1.14 (0.81, 1.64) |
| **Number of CSVD markers** |
| **3 vs. 0-2** | 1.31 (0.62, 2.75) | **1.17** **(1.12, 1.23) \*\*\*** | 1.10 (0.93, 1.30) | 0.98 (0.93, 1.02) | 1.00 (0.93, 1.07) | 1.06 (0.97, 1.16) | **0.97** **(0.95, 1.00) \*** | 1.01 (0.97, 1.06) | 1.00 (0.98, 1.01) | 1.01 (0.98, 1.05) | 1.00 (0.99, 1.01) | 1.00 (0.98, 1.02) | 1.00 (1.00, 1.01) | 1.02 (0.72, 1.48) | 1.05 (0.96, 1.15) | 1.31 (0.75, 2.35) |
| **4 vs. 0-2** | 0.90 (0.38, 2.12) | **1.18** **(1.13, 1.25) \*\*\*** | 1.05 (0.88, 1.27) | 0.96 (0.91, 1.02) | 0.98 (0.91, 1.06) | 1.05 (0.96, 1.16) | 0.98 (0.96, 1.01) | 1.05 (1.00, 1.10) | 1.00 (0.98, 1.01) | 1.01 (0.98, 1.06) | 1.00 (0.99, 1.00) | 1.01 (0.99, 1.03) | 1.00 (1.00, 1.00) | 0.93 (0.61, 1.41) | 1.11 (1.00, 1.23) | 1.20 (0.62, 2.40) |

OR (95% confidence interval). WMH, white matter hyperintensities; EPVS, enlarged perivascular space; CMBs, cerebral microbleeds.

Table S2：abbreviations

|  |  |
| --- | --- |
| **abbreviations** | **Full title**  |
| ALP | alkaline phosphatase |
| ALT | alanine aminotransferase |
| AST | aspartate aminotransferase |
| BMI | body mass index |
| BUN | urea nitrogen  |
| CMBs | cerebral microbleeds |
| CR | serum creatinine |
| CSVD | cerebral small vessel disease |
| DBP | diastolic blood pressure |
| EPVS | enlarged perivascular space |
| FBG | fasting blood glucose |
| FLAIR | fluid-attenuated inversion recovery |
| GGT | gamma-glutamyl Transferase |
| GMV | gray matter volume |
| HbA1c | hemoglobin A1c |
| HDL-c | HDL-cholesterol |
| LDL-c | LDL-cholesterol |
| MMSE | Mini-Mental State Examination |
| MoCA | Montreal Cognitive Assessment |
| MRI | magnetic resonance imaging |
| PBG | post-load blood glucose |
| PC MRA | phase contrast magnetic resonance angiography |
| SBP | systolic blood pressure |
| SWI | susceptibility weighted imaging |
| TC | total cholesterol |
| TG | triacylglycerol |
| TIV | total intracranial volume |
| UA | uric acid |
| VBM | voxel-based morphometry |
| VIF | variance inflation factor |
| WHR | waist-to-hip ratio |
| WMH | white matter hyperintensities |
| WMV | white matter volume |

Table S3: Group comparison between brain atrophy and normal participants

|  |  |  |  |
| --- | --- | --- | --- |
|  | Brain atrophy | Normal | P value |
| N | 465 | 50 |  |
| GMV | 601.11 (62.77) | 638.53 (51.78) | <0.001 |
| WMV | 406.64 (48.40) | 416.94 (44.03) | 0.125 |
| GMV+WMV | 1007.75 (98.37) | 1055.47 (87.74) | 0.001 |

Mean (SD). N: number of participants; GMV: gray matter volume; WMV: white matter volume.