| Sunnlementary Ta | hle 4 Com | narison of demographic and | d clinical data between N | I natients who never | had a stroke and the other pa | atients |
|------------------|-----------|-----------------------------|---------------------------|-------------------------|-------------------------------|---------|
| Supplementary la | | parison of uchiographic and | u ciinicai uata octween n | vint patients who never | nau a shoke anu the other pa | aucius |

| Variable | N_{int} patients who never had a stroke (n=12) | The other patients (n=117) | Р |
|--|--|----------------------------|--------|
| Age at inclusion (yr) | 64 (60–68) | 66 (61–70) | 0.305 |
| Age at last visit (yr) | 70 (67–72) | 72 (68–75) | 0.154 |
| Female sex | 8 (66.7) | 70 (59.8) | 0.763 |
| Education (yr) | 12 (9–17) | 9 (6–12) | 0.056 |
| Vascular risk factors | | | |
| Hypertension | 3 (25) | 33 (28.2) | 0.557 |
| Diabetes mellitus | 1 (8.3) | 12 (10.3) | 1.000 |
| Hypercholesterolemia | 4 (33.3) | 62 (53.0) | 0.160 |
| Smoking | 2 (16.7) | 6 (5.1) | 0.162 |
| Alcohol consumption | 2 (16.7) | 50 (42.7) | 0.210 |
| Clinical manifestations | | | |
| Migraine with aura | 8 (66.7) | 39 (33.3) | 0.030 |
| Migraine without aura | 6 (50.0) | 23 (19.7) | 0.027 |
| Stroke | 0 (0) | 86 (73.5) | <0.001 |
| Any cognitive complaints | 0 (0) | 67 (57.3) | <0.001 |
| Dementia | 0 (0) | 17 (14.5) | 0.365 |
| Transient episode of mood disturbance | 3 (25.0) | 48 (41.0) | 0.362 |
| Seizures | 0 (0) | 14 (12.0) | 0.360 |
| Clinical scales | | | |
| Severe disability preventing cognitive testing | 0 (0) | 15 (12.8) | 0.360 |
| mRS | 1 (1–1) | 2 (1–3) | <0.001 |
| Barthel index | 100 (100–100) | 95 (60–100) | 0.001 |
| NIHSS | 0 (0–0) | 1 (0–3) | <0.001 |
| MMSE | 29 (27–30) | 25 (20–28) | <0.001 |
| MDRS | 142 (139–143) | 130 (109–138) | <0.001 |
| EGFr domain 1-6 | 7 (58.3) | 57 (48.7) | 0.560 |

Values are presented as median (interquartile range) or number (%).

N_{int}, neurologically intact; mRS, modified Rankin Scale; NIHSS, National Institutes of Health Stroke Scale; MMSE, Mini-Mental State Examination; MDRS, Mattis Dementia Rating Scale; EGFr, epidermal growth factor-like repeat.

Supplementary Table 5. Comparison of imaging data between N_{int} patients who never had a stroke and the other patients

| | N_{int} patients who never had a stroke (n=12) | The other patients (n=107) | Р |
|------------------------------------|--|----------------------------|--------|
| Brain parenchymal fraction (%) | 81.9 (78.4–83.5) | 77.1 (73.9–79.7) | <0.001 |
| WMHs volume (mL) | 112.6 (57.7–162.8) | 97.6 (57.5–149.2) | 0.881 |
| Normalized WMHs (%) | 7.8 (3.8–11.5) | 6.4 (4.2–11.2) | 0.832 |
| Fazekas periventricular WMHs score | 3 (3–3) | 3 (3–3) | 1.000 |
| Fazekas deep WMHs score | 3 (3–3) | 3 (3–3) | 0.596 |
| Score of WMHs in temporal poles | 2 (1–3) | 3 (1–3) | 0.384 |
| Presence of lacune | 7 (58.3) | 97 (90.7) | 0.008 |
| Total lacune number | 1 (0–3) | 10 (4–16) | <0.001 |
| Presence of microbleeds | 2 (16.7) | 83 (77.6) | <0.001 |
| Total microbleeds number | 0 (0–0) | 5 (1–23) | <0.001 |
| Presence of RSSI | 0 (0) | 20 (18.7) | 0.214 |

Values are presented as median (interquartile range) or number (%). In 10 patients of the N_{ps} group imaging data could not be assessed (two patients did not have magnetic resonance imaging at day of clinical examination, in seven cases imaging data were of poor quality, in another case errors were detected using the Brain Intensity AbNormality Classification Algorithm [BIANCA] processing).

N_{int}, neurologically intact; WMH, white matter hyperintensity; RSSI, recent small subcortical infarct; N_{pst} with permanent neurological symptoms.