**Supplementary material**

**Supplementary Table 1**

Results of the linear mixed model with BPF as dependent variable and baseline pCBF as independent variable assuming a fixed slope with time. Estimates represent fixed effects of the linear mixed model with their 95% confidence intervals for a 1 unit increase of a continuous variable or presence of a dichotomous variable unless stated otherwise.

| Model                          | Estimate (95% CI)       | p value |
|-------------------------------|------------------------|---------|
| Intercept                     | 78.40 (77.50 to 79.30) | <0.001 |
| Baseline pCBF \(^a\)          | -0.10 (-0.22 to 0.02)  | 0.096   |
| Rate of change                |                        |         |
| Time \(^b\)                   | -0.23 (-0.24 to -0.22) | <0.001  |
| Time x baseline pCBF          | -0.01 (-0.02 to -0.003)| 0.007   |
| Age \(^b\)                    | -0.05 (-0.07 to -0.03) | <0.001  |
| Sex \(^c\)                    | 0.84 (0.53 to 1.15)    | <0.001  |
| Large infarcts on MRI         | -0.64 (-1.04 to -0.25) | 0.001   |
| Lacunes on MRI                | -0.54 (-0.87 to -0.21) | 0.001   |
| WMH volume on MRI \(^d\)      | -0.02 (-0.12 to 0.09)  | 0.748   |
| Hypertension                  | -0.21 (-0.45 to 0.03)  | 0.087   |
| Diabetes mellitus             | -1.04 (-1.34 to -0.74) | <0.001  |
| Carotid stenosis ≥70%         | -0.16 (-0.59 to 0.27)  | 0.465   |
| Body mass index               | 0.03 (-0.00 to 0.06)   | 0.082   |
| Smoking pack years            | -0.01 (-0.02 to -0.01) | <0.001  |
| Alcohol use                   |                        |         |
| Current                       | 0 (reference)          | -       |
| Former                        | -0.44 (-0.86 to -0.01) | 0.043   |
| Never                         | 0.11 (-0.22 to 0.44)   | 0.522   |

\(^a\) Per standard deviation decrease.

\(^b\) Per year increase.

\(^c\) Females vs. males.

\(^d\) Natural log-transformed due to a non-normal distribution and normalized for total intracranial volume.

BPF: brain parenchymal fraction, pCBF: parenchymal cerebral blood flow, CI: confidence interval, WMH: white matter hyperintensity.
Supplementary Table 2

Results of the linear mixed model with BPF as dependent variable and baseline pCBF as independent variable in patients without missing data. Estimates represent fixed effects of the linear mixed model with their 95% confidence intervals for a 1 unit increase of a continuous variable or presence of a dichotomous variable unless stated otherwise.

| Model                      | Estimate (95% CI)    | p value |
|----------------------------|---------------------|---------|
| Intercept                  | 78.69 (77.75 to 79.62) | <0.001 |
| Baseline pCBF a           | -0.12 (-0.25 to 0.00) | 0.053   |
| Rate of change             |                     |         |
| Time b                     | -0.24 (-0.25 to -0.22) | <0.001 |
| Time x baseline pCBF      | -0.01 (-0.02 to -0.003) | 0.011   |
| Age b                      | -0.05 (-0.07 to -0.03) | <0.001 |
| Sex c                      | 0.75 (0.43 to 1.08)  | <0.001 |
| Large infarcts on MRI     | -0.65 (-1.07 to -0.22) | 0.003   |
| Lacunes on MRI            | -0.56 (-0.91 to -0.21) | 0.002   |
| WMH volume on MRI d       | -0.01 (-0.11 to 0.10) | 0.907   |
| Hypertension              | -0.17 (-0.42 to 0.08) | 0.171   |
| Diabetes mellitus         | -1.09 (-1.40 to -0.77) | <0.001 |
| Carotid stenosis ≥70%     | -0.15 (-0.60 to 0.30) | 0.509   |
| Body mass index           | 0.02 (-0.01 to 0.06)  | 0.150   |
| Smoking pack years        | -0.01 (-0.02 to -0.01) | <0.001 |
| Alcohol use               |                     |         |
| Current                   | 0 (reference)       |         |
| Former                    | -0.44 (-0.86 to 0.01) | 0.054   |
| Never                     | 0.09 (-0.25 to 0.44) | 0.596   |

a Per standard deviation decrease.

b Per year increase.

c Females vs. males.

d Natural log-transformed due to a non-normal distribution and normalized for total intracranial volume.

BPF: brain parenchymal fraction, pCBF: parenchymal cerebral blood flow, CI: confidence interval, WMH: white matter hyperintensity.