

## 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)	<i>p</i> value
Intercept	78.40 (77.50 to 79.30)	<0.001
Baseline pCBF <sup>a</sup>	-0.10 (-0.22 to 0.02)	0.096
Rate of change		
Time <sup>b</sup>	-0.23 (-0.24 to -0.22)	<0.001
Time x baseline pCBF	-0.01 (-0.02 to -0.003)	0.007
Age <sup>b</sup>	-0.05 (-0.07 to -0.03)	<0.001
Sex <sup>c</sup>	0.84 (0.53 to 1.15)	<0.001
Large infarcts on MRI	-0.64 (-1.04 to -0.25)	0.001
Lacunae on MRI	-0.54 (-0.87 to -0.21)	0.001
WMH volume on MRI <sup>d</sup>	-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 $\geq 70\%$	-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

<sup>a</sup> Per standard deviation decrease.

<sup>b</sup> Per year increase.

<sup>c</sup> Females vs. males.

<sup>d</sup> 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)	<i>p</i> value
Intercept	78.69 (77.75 to 79.62)	<0.001
Baseline pCBF <sup>a</sup>	-0.12 (-0.25 to 0.00)	0.053
Rate of change		
Time <sup>b</sup>	-0.24 (-0.25 to -0.22)	<0.001
Time x baseline pCBF	-0.01 (-0.02 to -0.003)	0.011
Age <sup>b</sup>	-0.05 (-0.07 to -0.03)	<0.001
Sex <sup>c</sup>	0.75 (0.43 to 1.08)	<0.001
Large infarcts on MRI	-0.65 (-1.07 to -0.22)	0.003
Lacunae on MRI	-0.56 (-0.91 to -0.21)	0.002
WMH volume on MRI <sup>d</sup>	-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 $\geq 70\%$	-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

<sup>a</sup> Per standard deviation decrease.

<sup>b</sup> Per year increase.

<sup>c</sup> Females vs. males.

<sup>d</sup> 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.