**Supplementary materials (online only)**

Liver fibrosis, not steatosis, associates with long-term outcomes in ischaemic stroke patients

**Online Supplementary Contents**

# Supplementary methods

# Supplementary Table 1. Univariable proportional hazard models

# Supplementary methods

## *Clinical variables*

We collected patient data on vascular risk factors such as hypertension, diabetes, dyslipidemia, body mass index (BMI, kg/m2), metabolic syndrome according to National Cholesterol Education Program Expert Panel and Adult Treatment Panel III (NCEP - ATP III) criteria, current smoking, atrial fibrillation, and prior history of ischaemic heart disease, ischaemic stroke, or peripheral artery occlusive disease. We collected laboratory data including platelet count (×103/μL), aspartate aminotransferase (μkat/L), alanine aminotransferase (μkat/L), estimated glomerular filtration rate (mL/min/1.73 m2), total cholesterol (mmol/L), triglycerides (mmol/L), high-density cholesterol (mmol/L), low-density cholesterol (mmol/L), and fasting blood glucose (mmol/L). Stroke severity was assessed using the National Institute of Health Stroke Scale (NIHSS). Duration (days) of hospitalization at the department of neurology was also collected. The subtype of stroke was determined based on Trial of ORG 10172 in Acute Stroke Treatment (TOAST) classification [1].

## *Transient elastography evaluation*

Transient elastography (TE) was performed between the 5th and 7th intercostal spaces, at the mid-to-anterior axillary line, at least 10 times [2]. The TE results for the degree of liver fibrosis were expressed as kilopascals (kPa) for liver stiffness (LS). The median value of successful measurements was considered representative of the LS values for a given participant. LS measurement failures were defined as the absence of valid shots (i.e., valid shots = 0). A reliable LS value was defined by using the following three criteria: (i) at least 10 valid shots, and (ii) an interquartile range (IQR) 30% of the median LS value. Moreover, we collected data on the degree of liver steatosis, which was expressed as controlled attenuation parameter (CAP) values. The CAP measures the ultrasonic attenuations induced by liver steatosis at 3.5 MHz by using signals acquired by TE, and it is calculated simultaneously with the LS value by using the same signals.

# Supplementary Table 1. Univariable proportional hazard models

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | All-cause mortality | | Cardiovascular mortality | | Noncardiovascular mortality | |
|  | HR (95% CI) | *p* value | HR (95% CI) | *p* value | HR (95% CI) | *p* value |
| Age, yrs | 1.08 (1.04-1.13) | <0.001 | 1.07 (1.03-1.12) | 0.001 | 1.11 (1.02-1.21) | 0.012 |
| Sex, men | 0.76 (0.36-1.60) | 0.476 | 0.67 (0.28-1.60) | 0.367 | 1.09 (0.26-4.52) | 0.909 |
| Hypertension | 1.59 (0.60-4.18) | 0.348 | 1.96 (0.57-6.76) | 0.286 | 1.01 (0.20-5.02) | 0.988 |
| Diabetes | 1.14 (0.53-2.47) | 0.744 | 1.69 (0.70-4.07) | 0.244 | 0.28 (0.03-2.31) | 0.237 |
| Dyslipidemia | 0.36 (0.09-1.52) | 0.166 | 0.53 (0.12-2.24) | 0.386 | 0.00 (0.00-0.00) | <0.001 |
| Metabolic syndrome | 0.80 (0.38-1.68) | 0.550 | 0.92 (0.38-2.21) | 0.854 | 0.56 (0.13-2.32) | 0.421 |
| Ischaemic heart disease | 0.59 (0.26-1.35) | 0.213 | 0.64 (0.25-1.66) | 0.357 | 0.51 (0.10-2.48) | 0.402 |
| Prior history of ischaemic stroke | 1.12 (0.45-2.76) | 0.807 | 1.03 (0.35-3.01) | 0.956 | 1.38 (0.28-6.66) | 0.691 |
| Peripheral artery occlusive disease | 3.18 (1.35-7.47) | 0.008 | 4.13 (1.60-10.63) | 0.003 | 1.22 (0.15-9.94) | 0.853 |
| Atrial fibrillation | 1.45 (0.62-3.41) | 0.394 | 1.09 (0.36-3.23) | 0.883 | 2.57 (0.60-11.02) | 0.202 |
| Smoker | 0.27 (0.06-1.12) | 0.070 | 0.39 (0.09-1.67) | 0.204 | 0.00 (0.00-0.00) | <0.001 |
| Body mass index, kg/m2 | 0.80 (0.70-0.91) | 0.001 | 0.80 (0.70-0.91) | 0.001 | 0.82 (0.67-1.00) | 0.049 |
| NIHSS | 1.08 (1.02-1.15) | 0.010 | 1.08 (1.01-1.16) | 0.028 | 1.09 (1.00-1.17) | 0.037 |
| Duration of hospitalization, day | 1.06 (1.03-1.08) | <0.001 | 1.06 (1.03-1.09) | <0.001 | 1.04 (0.99-1.08) | 0.089 |
| Stroke mechanism, CE | 1.39 (0.52-3.70) | 0.511 | 1.38 (0.55-3.46) | 0.494 | 2.28 (0.54-9.57) | 0.259 |
| Aspartate aminotransferase, μkat/L | 1.24 (0.48-3.20) | 0.660 | 1.11 (0.53-2.32) | 0.784 | 1.59 (0.88-2.87) | 0.127 |
| Alanine aminotransferase, μkat/L | 0.16 (0.01-1.79) | 0.136 | 0.01 (0.00-1.57) | 0.071 | 1.18 (0.38-3.69) | 0.777 |
| Platelet count, ×103/μL | 0.99 (0.98-1.00) | 0.002 | 0.99 (0.98-1.00) | 0.110 | 0.99 (0.97-1.01) | 0.301 |
| eGFR, mL/min/1.73 m2 | 0.97 (0.96-0.98) | <0.001 | 0.96 (0.94-0.97) | <0.001 | 1.04 (0.99-1.09) | 0.120 |
| Total cholesterol, mmol/L | 1.02 (0.90-1.16) | 0.733 | 1.03 (0.95-1.12) | 0.480 | 0.99 (0.88-1.13) | 0.932 |
| Triglycerides, mmol/L | 1.04 (0.73-1.47) | 0.840 | 1.15 (0.94-1.40) | 0.165 | 0.43 (0.14-1.38) | 0.159 |
| High density lipoprotein, mmol/L | 0.27 (0.06-1.23) | 0.092 | 0.05 (0.01-0.37) | 0.003 | 2.79 (0.70-11.10) | 0.146 |
| Low density lipoprotein, mmol/L | 1.20 (0.84-1.70) | 0.311 | 1.28 (0.77-2.11) | 0.345 | 0.99 (0.66-1.48) | 0.945 |
| Fasting blood glucose, mmol/L | 1.04 (0.95-1.14) | 0.382 | 1.06 (0.96-1.16) | 0.253 | 0.96 (0.80-1.15) | 0.684 |
| Liver stiffness, kPa | 1.08 (1.04-1.12) | <0.001 | 1.09 (1.03-1.15) | 0.001 | 1.05 (1.00-1.10) | 0.050 |
| No fibrosis | 1 |  | 1 |  | 1 |  |
| Minimal fibrosis | 2.56 (1.06-6.17) | 0.037 | 1.89 (0.76-4.73) | 0.173 | 1.15 (0.23-5.76) | 0.865 |
| Significant fibrosis | 5.52 (2.22-13.72) | <0.001 | 3.27 (1.17-9.08) | 0.023 | 5.58 (1.36-22.89) | 0.017 |
| CAP, dB/m | 0.99 (0.98-1.00) | 0.011 | 0.99 (0.98-1.00) | 0.027 | 0.99 (0.98-1.01) | 0.237 |
| Fatty liver, >250.0 dB/m | 0.45 (0.19-1.06) | 0.069 | 0.46 (0.17-1.26) | 0.132 | 0.45 (0.09-2.25) | 0.329 |

The Cox regression for all-cause mortality, and Fine and Gray’s modified Cox regression for cardiovascular mortality and noncardiovascular mortality were applied to calculate proportional hazard ratios (HR) with 95% confidence intervals (CI). HR, hazards ratio; CI, confidence interval; NIHSS, National Institute of Health Stroke Scale; CE, cardioembolism; eGFR, estimated glomerular filtration rate; CAP, Controlled attenuation parameter.

1 Adams HP, Jr., Bendixen BH, Kappelle LJ, Biller J, Love BB, Gordon DL, et al: Classification of subtype of acute ischemic stroke. Definitions for use in a multicenter clinical trial. Toast. Trial of org 10172 in acute stroke treatment. Stroke 1993;24:35-41.

2 Kim SU, Kim JK, Park JY, Ahn SH, Lee JM, Baatarkhuu O, et al: Variability in liver stiffness values from different intercostal spaces. Liver Int 2009;29:760-766.