**Supplementary Table 1**. Pearson correlations of nine amino acids with clinical and laboratory measurements

|  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Amino acid | BMI | Waist | Systolic BP | LDL-C | Total Triglys | FPG | 2hPG | FPI | 2hPI | hs-CRP | MatsudaISI |
| Alanine | 0,253\*\* | 0,266\*\* | 0,171\*\* | 0,023\* | 0,385\*\* | 0,259\*\* | 0,234\*\* | 0,380\*\* | 0,330\*\* | 0,072\*\* | -0,395\*\* |
| Glutamine | -0,183\*\* | -0,194\*\* | -0,078\*\* | -0,073\*\* | -0,182\*\* | -0,200\*\* | -0,148\*\* | -0,213\*\* | -0,084\*\* | -0,213\*\* | 0,192\*\* |
| Glycine | -0,102\*\* | -0,105\*\* | -0,009 | -0,042\*\* | -0,060\*\* | -0,011 | -0,084\*\* | -0,080\*\* | -0,085\*\* | -0,017 | 0,101\*\* |
| Histidine | -0,036\*\* | -0,050\*\* | -0,050\*\* | 0,064\*\* | 0,050\*\* | -0,083\*\* | -0,057\*\* | -0,028\*\* | 0,025\* | -0,149\*\* | -0,008 |
| Isoleucine | 0,378\*\* | 0,370\*\* | 0,096\*\* | 0,107\*\* | 0,729\*\* | 0,230\*\* | 0,252\*\* | 0,475\*\* | 0,432\*\* | 0,159\*\* | -0,502\*\* |
| Leucine | 0,352\*\* | 0,331\*\* | 0,085\*\* | 0,103\*\* | 0,536\*\* | 0,222\*\* | 0,213\*\* | 0,402\*\* | 0,349\*\* | 0,180\*\* | -0,415\*\* |
| Phenylalanine | 0,317\*\* | 0,328\*\* | 0,127\*\* | 0,053\*\* | 0,265\*\* | 0,138\*\* | 0,191\*\* | 0,355\*\* | 0,302\*\* | 0,384\*\* | -0,365\*\* |
| Tyrosine | 0,348\*\* | 0,336\*\* | 0,138\*\* | 0,007 | 0,258\*\* | 0,164\*\* | 0,186\*\* | 0,407\*\* | 0,333\*\* | 0,177\*\* | -0,420\*\* |
| Valine | 0,291\*\* | 0,256\*\* | 0,018 | 0,020 | 0,164\*\* | 0,163\*\* | 0,105\*\* | 0,326\*\* | 0,264\*\* | 0,121\*\* | -0,307\*\* |

\**P*< 0.05, \*\* *P*<0.01

Abbreviations, BMI, body mass index; BP, blood pressure, Triglys, triglycerides; FPG, fasting plasma glucose, 2hPG, 2-hour plasma glucose, FPI, fasting plasma insulin; 2hPI, 2-hour plasma insulin; hs-CRP, high-sensitivity C-reactive protein, Matsuda ISI, Matsuda insulin sensitivity index.

**Supplementary Table 2**. Hazard ratios and their 95% CI for the association of nine amino acids

with the risk of coronary artery disease, ischemic stroke and cardiovascular events

|  |  |  |  |
| --- | --- | --- | --- |
| **Coronary Artery Disease** |   |   |   |
| **Amino acid** | **Cases N** | **Total N** | **HR** | ***P*** | ***P*\*** |
| Alanine | 661 | 9707 | 1,11 (1,03 - 1,20) | **5,0E-10** | **0,021** |
| Glutamine | 661 | 9694 | 0,92 (0,85 - 0,99) | **9,3E-05** | **0,026** |
| Glycine | 659 | 9680 | 1,02 (0,95 - 1,10) | 0,583 | 0,569 |
| Histidine | 662 | 9713 | 0,97 (0,90 - 1,05) | **0,003** | 0,637 |
| Isoleucine | 661 | 9705 | 1,07 (0,98 - 1,18) | **1,6E-07** | 0,166 |
| Leucine | 658 | 9671 | 1,06 (0,97 - 1,15) | **2,5E-04** | 0,216 |
| Phenylalanine | 661 | 9700 | 1,21 (1,12 - 1,31) | **1,3E-18** | **5,0E-06** |
| Tyrosine | 662 | 9712 | 1,15 (1,06 - 1,25) | **3,6E-08** | **0,002** |
| Valine | 662 | 9713 | 1,00 (0,92 - 1,08) | **0,037** | 0,807 |
| **Ischemic stroke** |   |   |   |  |
| Alanine | 394 | 9911 | 1,02 (0,92 - 1,14) | **0,002** | 0,799 |
| Glutamine | 394 | 9896 | 0,86 (0,78 - 0,95) | **1,8E-04** | **0,003** |
| Glycine | 392 | 9882 | 0,99 (0,90 - 1,09) | 0,951 | 0,896 |
| Histidine | 394 | 9917 | 0,91 (0,83 - 1,01) | **4,4E-05** | 0,096 |
| Isoleucine | 393 | 9908 | 1,02 (0,90 - 1,15) | 0,128 | 0,861 |
| Leucine | 392 | 9875 | 1,00 (0,89 - 1,12) | 0,613 | 0,922 |
| Phenylalanine | 394 | 9902 | 1,24 (1,13 - 1,37) | **1,4E-12** | **1,5E-05** |
| Tyrosine | 394 | 9916 | 1,11 (1,00 - 1,24) | **0,003** | 0,084 |
| Valine | 394 | 9917 | 1,00 (0,90 - 1,12) | 0,333 | 0,985 |
| **Cardiovascular disease** |   |   |  |
| Alanine | 965 | 9538 | 1,06 (0,99 - 1,13) | **7,0E-09** | 0,143 |
| Glutamine | 965 | 9525 | 0,91 (0,85 - 0,97) | **9,2E-06** | **0,004** |
| Glycine | 961 | 9511 | 1,02 (0,96 - 1,08) | 0,508 | 0,583 |
| Histidine | 966 | 9544 | 0,95 (0,89 - 1,02) | **1,7E-05** | 0,196 |
| Isoleucine | 965 | 9536 | 1,03 (0,96 - 1,12) | **2,0E-05** | 0,476 |
| Leucine | 962 | 9505 | 1,03 (0,96 - 1,11) | **0,005** | 0,436 |
| Phenylalanine | 965 | 9531 | 1,22 (1,14 - 1,30) | **1.3E-18** | **4,5E-09** |
| Tyrosine | 966 | 9543 | 1,13 (1,06 - 1,21) | **8,4E-09** | **0,001** |
| Valine | 966 | 9544 | 1,00 (0,93 - 1,07) | 0,050 | 0,871 |

*P*<0.05 in bold. *P*<0.0056 in bold and underlined

*P* is based on an unadjusted Cox regression model. HR and *P*\* values were adjusted for age, diabetes status, fasting insulin, smoking, BMI, LDL cholesterol, HDL cholesterol, drug treatment for hypertension, high sensitivity C–reactive protein, and statin treatment.