|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Amino acid | Early-stage |  | Late-stage | FoldChange e | *P*-value e | *P*-FDR e |
| N=85 |  | N=103 |
| Median | IQR | FoldChange c | *P*-value c | *P*-FDR c |  | Median | IQR | FoldChange d | *P*-value d | *P*-FDR d |
| Phenylalanine a | 96.90  | 40.10  | 1.00  | 0.800  | 0.838  |  | 112.00  | 46.20  | 1.16  | <0.001 | **<0.001** | 1.16 | 0.004  | 0.088  |
| Tryptophan a | 51.90  | 26.70  | 0.90 | 0.055  | 0.152  |  | 51.10  | 23.90  | 0.89 | 0.024  | **0.048**  | 0.98 | 0.929  | 0.929  |
| Isoleucine a | 84.50  | 43.70  | 1.03  | 0.168  | 0.264  |  | 88.40  | 36.30  | 1.08  | 0.021  | **0.048** | 1.05  | 0.582  | 0.800  |
| Leucine a | 170.00  | 66.00  | 1.06  | 0.434  | 0.617  |  | 173.00  | 60.00  | 1.07  | 0.027  | 0.050  | 1.02  | 0.341  | 0.757  |
| Methionine a | 27.80  | 11.90  | 0.94 | 0.496  | 0.633  |  | 27.70  | 11.40  | 0.93 | 0.714  | 0.827  | 1.00  | 0.784  | 0.862  |
| Lysine a | 237.00  | 120.00  | 1.07  | 0.158  | 0.264  |  | 222.00  | 116.50  | 1.00  | 0.810  | 0.849  | 0.94  | 0.283  | 0.757  |
| Valine a | 295.00  | 130.50  | 1.07  | 0.449  | 0.617  |  | 290.00  | 99.50  | 1.05  | 0.164  | 0.241  | 0.98  | 0.712  | 0.862  |
| Threonine a | 152.00  | 84.00  | 1.03  | 0.091  | 0.174  |  | 150.00  | 75.00  | 1.01  | 0.860  | 0.860  | 0.99  | 0.216  | 0.679  |
| Glycine b | 342.00  | 178.50  | 1.05  | 0.095  | 0.174  |  | 367.00  | 171.50  | 1.13  | 0.002  | **0.007**  | 1.07  | 0.437  | 0.757  |
| Serine b | 185.00  | 88.50  | 1.08  | 0.069  | 0.152  |  | 191.00  | 72.50  | 1.12  | 0.003  | **0.009**  | 1.03  | 0.462  | 0.757  |
| Asparagine b | 61.40  | 27.90  | 1.06  | 0.041  | 0.152  |  | 63.70  | 22.10  | 1.10  | 0.009  | **0.025**  | 1.04  | 0.765  | 0.862  |
| Aspartic acid b | 40.40  | 32.50  | 1.24  | 0.001  | 0.022  |  | 50.30  | 34.20  | **1.55**  | <0.001 | **<0.001** | 1.25  | 0.008  | 0.088  |
| Cysteine b | 64.50  | 45.20  | 1.20  | 0.032  | 0.152  |  | 72.70  | 54.20  | **1.35**  | <0.001 | **<0.001** | 1.13  | 0.122  | 0.447  |
| Glutamic acid b | 119.00  | 70.00  | 1.14  | 0.004  | **0.044** |  | 136.00  | 82.00  | **1.30**  | <0.001 | **<0.001** | 1.14  | 0.089  | 0.392  |
| Glutamine b | 541.00  | 256.00  | 1.07  | 0.043  | 0.152  |  | 516.00  | 194.50  | 1.02  | 0.333  | 0.458  | 0.95  | 0.391  | 0.757  |
| Histidine b | 66.20  | 32.50  | 1.10  | 0.068  | 0.152  |  | 58.30  | 31.20  | 0.97 | 0.461  | 0.597  | 0.88  | 0.026  | 0.191  |
| Proline b | 209.00  | 123.50  | 0.98 | 0.855  | 0.855  |  | 225.00  | 90.50  | 1.05  | 0.123  | 0.193  | 1.08  | 0.403  | 0.757  |
| Arginine b | 104.00  | 64.60  | 0.97 | 0.746  | 0.821  |  | 121.00  | 77.20  | 1.13  | 0.023  | **0.048**  | 1.16  | 0.037  | 0.204  |
| Tyrosine b | 66.60  | 54.70  | 0.92 | 0.727  | 0.821  |  | 77.50  | 50.30  | 1.07  | 0.629  | 0.769  | 1.16  | 0.501  | 0.757  |
| Alanine b | 475.00  | 229.00  | 1.00  | 0.518  | 0.633  |  | 471.00  | 237.00  | 0.99  | 0.757  | 0.833  | 0.99  | 0.745  | 0.862  |
| Ornithine b | 111.00  | 96.90  | 1.20  | 0.011  | 0.081  |  | 115.00  | 71.90  | **1.24**  | <0.001 | **<0.001** | 1.04  | 0.516  | 0.757  |
| Citrulline b | 30.20  | 20.30  | 1.13  | 0.059 | **0.152** |  | 30.90 | 18.00 | 1.16 | 0.050 | 0.085  | 1.02 | 0.858 | 0.899  |

a essential amino acids.

b not essential amino acids.

c compared between early-stage and control.

d compared between late-stage and control.

e compared between early-stage and late-stage.

Mann-Whitney U test was used for continuous variables that did not normally distributed.

Benjamini-Hochberg procedure was used for multiple testing correction.