**Supplementary Table 1. Comparison of baseline characteristics between the 99 patients of the present study and the remaining 118 patients that were diagnosed with ALS and progressive spinal muscular atrophy during 2015-2018 in Stockholm**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Characteristics** | **Patients of the present study;**  **N=99** | **Remaining patients; N=118** | **Difference** | **P value\*** |
| Age at diagnosis, years |  |  |  |  |
| Mean (SD) | 65.72 (10.09) | 66.56 (11.83) | -0.84 | 0.57 |
| Diagnostic delay, months |  |  |  |  |
| Median (IQR) | 12.97 (8.60-19.10) | 12.35 (6.90-20.80) | 0.62 | 0.20 |
| BMI at diagnosis |  |  |  |  |
| Median (IQR) | 24.38 (22.22-26.67) | 22.89 (20.32-27.16) | 1.49 | <0.01 |
| ALSFRS-R at diagnosis |  |  |  |  |
| Median (IQR) | 39.00 (32.50-43.50) | 36.00 (33.00-41.00) | 3 | 0.37 |
| Progression rate |  |  |  |  |
| Median (IQR) | 0.57 (0.29-1.05) | 0.61 (0.31-1.30) | -0.04 | 0.67 |
| Sex, % |  |  |  |  |
| Male | 52 (52.53) | 50 (42.37) |  | 0.14 |
| Female | 47 (47.47) | 68 (57.63) |  |
| Site of symptoms onset†, % |  |  |  |  |
| Bulbar | 38 (38.38) | 32 (32.65) |  | 0.40 |
| Non-bulbar | 61 (61.62) | 66 (67.35) |  |
| No. of patients died during follow-up | 54 | 53 |  |  |
| Mortality rate per 1000 person-months | 37.5 | 34.8 | 2.7 | 0.70 |
| \*Two-sample t-test for parametric variables, two-sample Kolmogorov-Smirnov test for nonparametric variables, Chi-square test for categorical variables, and Wald test for mortality rate.  †Information on site of symptoms onset was missing for 20 patients among the remaining patients. | | | | |

**Supplementary Table 2. Associations of lipids and apolipoproteins (per standard deviation increase) with risk of mortality after ALS diagnosis, with adjustment of sex, age at diagnosis, site of symptoms onset, diagnostic delay, BMI at diagnosis, ALSFRS-R at diagnosis, progression rate, and standard bicarbonate**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **Person-months** | **No. of deceased patients** | **HR (95% CI)** | **P value** |
| **Biomarkers of lipid metabolism** | |  |  |  |
| TC | 1312 | 45 | 0.62 (0.41-0.93) | 0.02 |
| HDL-C | 1312 | 45 | 1.19 (0.83-1.71) | 0.34 |
| LDL-C | 1273 | 44 | 0.65 (0.44-0.95) | 0.03 |
| LDL-C/HDL-C ratio | 1273 | 44 | 0.62 (0.43-0.89) | 0.01 |
| TG | 1312 | 45 | 0.80 (0.52-1.25) | 0.33 |
| **Biomarkers of apolipoprotein metabolism** | | |  |  |
| ApoA-I | 1355 | 47 | 1.25 (0.89-1.75) | 0.21 |
| ApoB | 1355 | 47 | 0.62 (0.43-0.89) | 0.01 |
| ApoB/ApoA-I ratio | 1355 | 47 | 0.58 (0.40-0.83) | <0.01 |
| HR = hazard ratio; CI = confidence interval; TC = total cholesterol; TG = triglycerides; HDL-C = high-density lipoprotein cholesterol; LDL-C = low-density lipoprotein cholesterol; ApoA-I = Apolipoprotein A-I; ApoB = Apolipoprotein B | | | | |

**Supplementary Table 3. Sensitivity analysis using the mean, 25th percentile, and 75th percentile values of the entire sample to replace missing values in Cox model, HR per standard deviation increase**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | **Mean** | | **25th percentile** | | **75th percentile** | |
|  | **HR (95% CI)** | **P value** | **HR (95% CI)** | **P value** | **HR (95% CI)** | **P value** |
| **Biomarkers of lipid metabolism** | | |  |  |  |  |
| TC | 0.60 (0.41-0.88) | <0.01 | 0.58 (0.39-0.85) | 0.01 | 0.64 (0.44-0.93) | 0.02 |
| HDL-C | 1.12 (0.79-1.58) | 0.52 | 1.07 (0.76-1.51) | 0.70 | 1.16 (0.82-1.63) | 0.41 |
| LDL-C | 0.64 (0.45-0.90) | 0.01 | 0.61 (0.43-0.86) | 0.01 | 0.68 (0.49-0.96) | 0.03 |
| LDL-C/HDL-C ratio | 0.65 (0.47-0.91) | 0.01 | 0.64 (0.45-0.88) | 0.01 | 0.69 (0.50-0.95) | 0.02 |
| TG | 0.87 (0.58-1.31) | 0.51 | 0.83 (0.55-1.26) | 0.39 | 0.90 (0.61-1.33) | 0.61 |
| **Biomarkers of apolipoprotein metabolism** | | | |  |  |  |
| ApoA-I | 1.18 (0.85-1.64) | 0.33 | 1.17 (0.84-1.62) | 0.36 | 1.18 (0.85-1.65) | 0.32 |
| ApoB | 0.63 (0.44-0.89) | <0.01 | 0.62 (0.44-0.88) | <0.01 | 0.64 (0.45-0.90) | 0.01 |
| ApoB/ApoA-I ratio | 0.61 (0.44-0.86) | <0.01 | 0.61 (0.43-0.86) | <0.01 | 0.62 (0.44-0.87) | 0.01 |
| HR = hazard ratio; CI = confidence interval; TC = total cholesterol; TG = triglycerides; HDL-C = high-density lipoprotein cholesterol; LDL-C = low-density lipoprotein cholesterol; ApoA-I = Apolipoprotein A-I; ApoB = Apolipoprotein B | | | | | | |

**Supplementary Table 4. Sensitivity analysis restricted to patients with lipids and apolipoproteins measured within one month from ALS diagnosis, HR per standard deviation increase**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **Person-months** | **No of deceased patients** | **HR (95% CI)** | **P value** |
| **Biomarkers of lipid metabolism** | | |  |  |
| TC | 728 | 29 | 0.53 (0.28-1.00) | 0.05 |
| HDL-C | 728 | 29 | 1.32 (0.83-2.12) | 0.24 |
| LDL-C | 708 | 29 | 0.71 (0.42-1.19) | 0.19 |
| LDL-C/HDL-C ratio | 708 | 29 | 0.63 (0.37-1.05) | 0.07 |
| TG | 728 | 29 | 0.46 (0.23-0.90) | 0.02 |
| **Biomarkers of apolipoprotein metabolism** | | | |  |
| ApoA-I | 735 | 29 | 1.76 (1.02-3.05) | 0.04 |
| ApoB | 735 | 29 | 0.66 (0.38-1.12) | 0.12 |
| ApoB/ApoA-I ratio | 735 | 29 | 0.52 (0.30-0.91) | 0.02 |
| HR = hazard ratio; CI = confidence interval; TC = total cholesterol; TG = triglycerides; HDL-C = high-density lipoprotein cholesterol; LDL-C = low-density lipoprotein cholesterol; ApoA-I = Apolipoprotein A-I; ApoB = Apolipoprotein B | | | | |

**Supplementary Table 5. Sensitivity analysis restricted to patients with ALS alone, HR per standard deviation increase**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **Person-months** | **No. of deceased patients** | **HR (95% CI)** | **P value** |
| **Biomarkers of lipid metabolism** | |  |  |  |
| TC | 1330 | 47 | 0.61 (0.41-0.90) | 0.01 |
| HDL-C | 1330 | 47 | 1.12 (0.78-1.61) | 0.54 |
| LDL-C | 1291 | 46 | 0.64 (0.45-0.93) | 0.02 |
| LDL-C/HDL-C ratio | 1269 | 46 | 0.66 (0.46-0.93) | 0.02 |
| TG | 1330 | 47 | 0.88 (0.58-1.33) | 0.53 |
| **Biomarkers of apolipoprotein metabolism** | | |  |  |
| ApoA-I | 1365 | 50 | 1.18 (0.85-1.65) | 0.33 |
| ApoB | 1365 | 50 | 0.62 (0.44-0.88) | 0.01 |
| ApoB/ApoA-I ratio | 1365 | 50 | 0.61 (0.43-0.86) | <0.01 |
| HR = hazard ratio; CI = confidence interval; TC = total cholesterol; TG = triglycerides; HDL-C = high-density lipoprotein cholesterol; LDL-C = low-density lipoprotein cholesterol; ApoA-I = Apolipoprotein A-I; ApoB = Apolipoprotein B | | | | |

**Supplementary Table 6. Sensitivity analysis using time since symptoms onset as the underlying time scale.**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **Person-months** | **No. of deceased patients** | **HR (95% CI)** | **P value** |
| **Biomarkers of lipid metabolism** | |  |  |  |
| TC | 2977 | 47 | 0.81 (0.56-1.18) | 0.01 |
| HDL-C | 2977 | 47 | 1.43 (1.00-2.05) | 0.05 |
| LDL-C | 2890 | 46 | 0.70 (0.49-1.00) | 0.05 |
| LDL-C/HDL-C ratio | 2837 | 46 | 0.62 (0.45-0.86) | <0.01 |
| TG | 2977 | 47 | 0.95 (0.66-1.38) | 0.80 |
| **Biomarkers of apolipoprotein metabolism** | | |  |  |
| ApoA-I | 3022 | 50 | 1.48 (1.06-2.05) | 0.02 |
| ApoB | 3022 | 50 | 0.72 (0.51-1.00) | 0.05 |
| ApoB/ApoA-I ratio | 3022 | 50 | 0.62 (0.45-0.85) | <0.01 |
| HR = hazard ratio; CI = confidence interval; TC = total cholesterol; TG = triglycerides; HDL-C = high-density lipoprotein cholesterol; LDL-C = low-density lipoprotein cholesterol; ApoA-I = Apolipoprotein A-I; ApoB = Apolipoprotein B | | | | |

**Supplementary Table 7. Area under the curve (AUC) from Cox model, with adjustment of sex, age at diagnosis, site of symptoms onset, diagnostic delay, BMI, ALSFRS-R score, and progression rate**

|  |  |
| --- | --- |
| **Different models** | **AUC** |
| Cox model without lipids or apolipoproteins | 0.8303 |
| Cox model including lipids | |
| TC | 0.8750 |
| HDL-C | 0.8377 |
| LDL-C | 0.8853 |
| LDL-C/HDL-C ratio | 0.8798 |
| TG | 0.8469 |
| Cox model including apolipoproteins | |
| ApoA-I | 0.8388 |
| ApoB | 0.8632 |
| ApoB/ApoA-I ratio | 0.8678 |
| TC = total cholesterol; TG = triglycerides; HDL-C = high-density lipoprotein cholesterol; LDL-C = low-density lipoprotein cholesterol; ApoA-I = Apolipoprotein A-I; ApoB = Apolipoprotein B | |