**Supplementary Information**

**Table A: Demographic characteristics of participants with NAFLD by fibrosis status based on NFS cutoffs in the U.S. National Health and Nutrition Examination Survey, 1999-2012**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Variable | NAFLD low risk of advanced fibrosis (n=739) | NAFLD indeterminate risk of advanced fibrosis (n=919) | NAFLD high risk of advanced fibrosis (n=245) | *p-*value1 | *p-*value2 | *p-value3* |
| Age (years) | 43.7 ± 13.2 | 58.8 ±14.2 | 67.9 ± 13.4 | <0.001 | <0.001 | <0.001 |
| Male | 61.8  | 58.7  | 51.6  | 0.282 | 0.015 | 0.140 |
| Ethnicity | <0.001 | <0.001 | 0.071 |
|  Non-Hispanic White | 72.1  | 81.3  | 83.8  |  |  |  |
|  Non-Hispanic Black | 5.6  | 5.5  | 7.5  |  |  |
|  Mexican American  | 13.1  | 6.1  | 5.6  |  |  |
|  Other Hispanic | 4.8  | 3.8  | 2.3  |  |  |
|  Other race | 4.6  | 3.4  | 0.8  |  |  |
| Foreign born | 17.1  | 10.9  | 6.4  | <0.001 | <0.001 | 0.023 |
| United States citizen | 89.8  | 95.2  | 97.5  | <0.001 | <0.001 | 0.041 |
| Served in the U.S. military | 11.2  | 24.1 | 28.4  | <0.001 | <0.001 | <0.001 |
| Income | 0.189 | <0.001 | 0.015 |
|  < $45,000  | 38.9  | 44.9  | 60.0  |  |  |  |
|  $45,000-74,999 | 26.6  | 22.9  | 20.2  |  |  |
|  ≥ $75,000 | 34.5  | 32.2 | 19.8  |  |  |
| Poverty income ratio < 1.0 | 12.8 | 8.5  | 9.0 | 0.460 | 0.170 | 0.828 |
| Marriage status | 0.011 | <0.001 | 0.140 |
|  Legally married | 67.3 | 70.4 | 58.6 |  |  |  |
|  Divorced/separated | 9.2 | 8.4 | 14.4 |  |  |
|  Never married | 14.6 | 8.3 | 3.8 |  |  |
|  Other | 8.9 | 13.0 | 23.2 |  |  |
| Smoking exposure | 0.005 | 0.031 | 0.848 |
|  Never | 63.8 | 54.9 | 54.1 |  |  |  |
|  Current/former | 36.2 | 45.1 | 45.9 |  |  |
| Education level | 0.981  | 0.029 | 0.023 |
|  ≤ High school | 59.5 | 59.4 | 49.2 |  |  |  |
|  > High school degree | 40.5 | 40.6 | 50.8 |  |  |

NFS (NAFLD fibrosis score, NFS = -1.675 + 0.037 x age(year) + 0.094 x BMI (kg/m2) + 1.13 x impaired fasting glycemia or diabetes (yes=1, no=0) + 0.99 x AST/ALT ratio - 0.013 x PLT (109/L) - 0.66 x ALB (g/dL); high risk of stage 3-4 (>0.676), indeterminate (0.676- -1.455), low risk of stage 3-4 (< -1.455)

1NAFLD low risk of fibrosis vs. NAFLD indeterminate risk of fibrosis

2NAFLD low risk of fibrosis vs. NAFLD high risk of fibrosis

3NAFLD indeterminate risk of fibrosis vs. NAFLD high risk of fibrosis

**Table B: Lab and clinical characteristics of participants by NAFLD and Fibrosis status based on NFS cutoffs in the U.S. National Health and Nutrition Examination Survey, 1999-2012**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Variable | NAFLD low risk of advanced fibrosis (n=739) | NAFLD indeterminate risk of advanced fibrosis (n=919) | NAFLD high risk of advanced fibrosis (n=245) | *p-*value1 | *p-*value2 | *p-*value3 |
| Hypertension | 15.6  | 24.6 | 26.9  | <0.001 | 0.003 | 0.584 |
| Hypercholesterolemia | 46.4  | 31.2 | 15.1  | <0.001 | <0.001 | <0.001 |
| Hyperlipidemia | 53.7  | 49.8 | 41.7  | 0.213 | 0.025 | 0.074 |
| Metabolic syndrome | 44.4  | 65.1 | 66.4  | <0.001 | <0.001 | 0.776 |
| Diabetes | 6.1  | 32.0 | 50.9  | <0.001 | <0.001 | <0.001 |
|  Controlled (HbA1c<6.5%) | 2.5  | 13.4 | 23.2  | <0.001 | <0.001 | <0.001 |
|  Uncontrolled (HbA1c≥6.5%) | 3.6  | 18.6 | 27.8  |  |  |  |
| Kidney failure | 0.8  | 2.5 | 5.0  | 0.011 | <0.001 | 0.060 |
| Asthma | 14.4 | 15.8 | 15.6 | 0.49 | 0.72 | 0.955 |
| Arthritis | 23.4 | 46.2 | 53.3 | <0.001 | <0.001 | 0.095 |
| Ischemic heart disease | 5.8 | 13.2 | 28.4 | <0.001 | <0.001 | <0.001 |
| Congestive heart failure | 1.9 | 4.9 | 11.6 | 0.010 | <0.001 | <0.001 |
| Stroke | 2.5 | 4.1 | 7.4 | 0.122 | 0.002 | 0.047 |
| Chronic obstructive pulmonary disease | 5.9 | 9.6 | 17.7 | 0.044 | <0.001 | 0.003 |
| Cancer | 5.7 | 15/3 | 26.8 | <0.001 | <0.001 | 0.002 |
| BMI (kg/m2) | 32.3 ± 5.4 | 34.4 ± 6.7 | 37.8 ± 10.0 | <0.001 | <0.001 | <0.001 |
| Waist circumference (cm) | 108.3 ± 12.0 | 114.3 ± 11.9 | 121.8 ± 19.0 | <0.001 | <0.001 | <0.001 |
| Albumin (g/dL) | 4.3 ± 0.3 | 4.2 ± 0.3 | 4.1 ± 0.3 | <0.001 | <0.001 | <0.001 |
| Alanine aminotransferase (U/L) | 35.8 ± 22.5 | 29.0 ± 14.9 | 25.4 ± 16.3 | <0.001 | <0.001 | 0.008 |
| Aspartate aminotransferase (U/L) | 27.5 ± 13.0 | 26.3 ± 11.3 | 27.4 ± 14.2 | 0.105 | 0.892 | 0.332 |
| Alkaline phosphatase (U/L) | 74.4 ± 19.7 | 73.1 ± 22.7 | 70.9 ± 28.1 | 0.302 | 0.057 | 0.243 |
| Gamma-glutamyl transferase (U/L) | 40.6 ± 31.9 | 35.6 ± 38.9 | 41.0 ± 59.5 | 0.013 | 0.907 | 0.108 |
| Platelet (109/L) | 292.9 ± 62.0 | 240.7 ± 53.8 | 197.9 ± 56.9 | <0.001 | <0.001 | <0.001 |
| Total bilirubin (mg/dL) | 0.74 ± 0.29 | 0.78 ± 0.31 | 0.80 ± 0.34 | 0.031 | 0.014 | 0.393 |
| Creatinine (mg/dL) | 0.87 ± 0.19 | 0.94 ± 0.36 | 1.05 ± 0.42 | <0.001 | <0.001 | 0.001 |
| HbA1c  | 5.6 ± 0.7 | 6.1 ± 1.3 | 6.4 ± 1.4 | <0.001 | <0.001 | 0.007 |
| Fasting glucose (mg/dL) | 104.0 ± 21.2 | 123.6 ± 42.1 | 130.7 ± 40.2 | <0.001 | <0.001 | 0.024 |
| Fasting insulin (uU/mL) | 20.1 ± 9.6 | 20.6 ± 12.5 | 26.3 ± 43.4 | 0.540 | <0.001 | 0.049 |
| HOMA-IR  | 5.2 ± 2.8 | 6.3 ± 4.7 | 8.6 ± 14.8 | <0.001 | 0.001 | 0.013 |
| Total cholesterol (mg/dL) | 208.8 ± 42.4 | 195.9 ± 42.3 | 179.6 ± 40.3 | <0.001 | <0.001 | <0.001 |
| HDL cholesterol (mg/dL) | 44.4 ± 10.8 | 45.6 ± 12.0 | 47.7 ± 13.3 | 0.060 | 0.003 | 0.034 |
| LDL cholesterol (mg/dL) | 126.8 ± 33.0 | 114.9 ± 35.7 | 101.2 ± 35.1 | <0.001 | <0.001 | <0.001 |
| Triglycerides (mg/dL) | 199.3 ± 145.2 | 180.4 ± 117.0 | 163.1 ± 112.1 | 0.039 | 0.001 | 0.027 |

NFS (NAFLD fibrosis score, NFS = -1.675 + 0.037 x age(year) + 0.094 x BMI (kg/m2) + 1.13 x impaired fasting glycemia or diabetes (yes=1, no=0) + 0.99 x AST/ALT ratio - 0.013 x PLT (109/L) - 0.66 x ALB (g/dL); high risk of stage 3-4 (>0.676), indeterminate (0.676- -1.455), low risk of stage 3-4 (< -1.455)

1NAFLD low risk vs. NAFLD indeterminate risk of advanced fibrosis

2NAFLD low risk vs. NAFLD high risk of advanced fibrosis

3NAFLD indeterminate risk vs. NAFLD high risk of advanced fibrosis

**Table C: Mortality in subjects by NAFLD status in the National Health and Nutrition Examination Survey 1999-2010**

|  |  |  |  |
| --- | --- | --- | --- |
| Variable | NAFLD  | No NAFLD | *p-*value |
| Months of follow up | 75.4 ± 42.7 | 80.7 ± 40.4 | 0.001 |
| **All-cause mortality (%)** | <0.001 |
|  5 year | 4.9 | 2.6 |  |
|  8 year | 9.4 | 5.5 |  |
| **Cardiovascular mortality (%)** | 0.049 |
|  5 year | 0.9 | 0.6 |  |
|  8 year | 1.5 | 1.0 |  |
| **Cancer mortality (%)** | 0.001 |
|  5 year | 1.5 | 0.6 |  |
|  8 year | 2.8 | 1.1 |  |

**Table D: Mortality by Fibrosis Status in subjects with NAFLD in the National Health and Nutrition Examination Survey 1999-2010**

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Variable | No NAFLD | NAFLD low risk advanced fibrosis | NAFLD indeterminate risk advanced fibrosis | NAFLD high risk advanced fibrosis | *p-*value1 | *p*-value2 | *p-* value3 | *p-* value4 |
| Months follow up | 80.7 ± 40.4 | 82.5 ± 39.1 | 71.6 ± 44.0 | 57.6 ± 44.0 | 0.390 | <0.001 | <0.001 | <0.001 |
| **All cause mortality (%)** | 0.015 | <0.001 | <0.001 | <0.001 |
| 5 year | 2.6 | 1.1 | 6.1 | 18.1 |  |
| 8 year | 5.5 | 2.8 | 11.6 | 35.0 |
| **Cardiovascular mortality (%)** | 0.001 | 0.003 | <0.001 | <0.001 |
| 5 year  | 0.6 | <0.1 | 1.0 | 5.1 |  |
| 8 year | 1.0 | <0.1 | 2.0 | 6.2 |
| **Cancer mortality (%)** | 0.700 | <0.001 | <0.001 | 0.009 |
| 5 year | 0.6 | 0.7 | 2.0 | 3.5 |  |
| 8 year | 1.1 | 1.4 | 3.8 | 5.9 |

1 No NAFLD vs low risk of advanced fibrosis

2No NAFLD vs indeterminate risk of advanced fibrosis

3 No NAFLD vs high risk

4 Low risk vs high risk of advanced fibrosis