**Table 1**.Baseline characteristics.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **Esophageal adenocarcinoma** | **Esophageal squamous-cell carcinoma** | **Gastric adenocarcinoma** | **Total cohort** |
| **Subject, n** | 62 | 64 | 373 | 192,903 |
| **Average follow up years (±std†)** | 6.9 (±3.8) | 5.1 (±3.6) | 5.9 (±3.9) | 10.6 (±4.0) |
| **Person years** | 428 | 325 | 1,612 | 2,050,335 |
| **Age at participation (±std†)** | 64.1 (±10.2) | 65.0 (±11.4) | 65.1 (±11.8) | 49.5 (±15.7) |
| **Sex, n (%)** |  |  |  |  |
| 1 Women | 7 (11.3%) | 27 (42.2%) | 153 (41.0%) | 99,845 (51.8%) |
| 2 Men | 55 (88.7%) | 37 (57.8%) | 220 (59.0%) | 93,058 (48.2%) |
| **BMI** |  |  |  |  |
| 1 (<25 kg/m2) | 8 (12.9%) | 32 (50.0%) | 136 (36.5%) | 83,542 (43.3%) |
| 2 (25-30 kg/m2) | 46 (74.2%) | 22 (34.4%) | 165 (44.2%) | 78,488 (40.7%) |
| 3 (≥30 kg/m2) | 8 (12.9%) | 10 (15.6%) | 72 (19.3%) | 29,667 (15.4%) |
| *Missing* | 0 | 0 | 0 | 1,206 (0.6%) |
| **Smoking status, n (%)** |  |  |  |  |
| 1 No | 43 (69.4%) | 25 (39.1%) | 250 (67.0%) | 129,363 (67.1%) |
| 2 Yes | 19 (30.6%) | 38 (59.4%) | 120 (32.2%) | 55,186 (28.6%) |
| *Missing* | 0 | 1 (1.5%) | 3 (0.8%) | 8,354 (4.3%) |
| **Education** |  |  |  |  |
| 1 (primary/secondary school) | 13 (21.0%) | 24 (37.5%) | 157 (42.1%) | 43,639 (22.6%) |
| 2 (high school) | 20 (32.2%) | 11 (17.2%) | 69 (18.5%) | 57,210 (30.6%) |
| 3 (university) | 4 (6.5%) | 5 (7.8%) | 23 (6.2%) | 21,137 (11.0%) |
| *Missing* | 25 (40.3%) | 24 (37.5%) | 124 (33.2%) | 70,917 (36.8%) |
| **Family cancer history** |  |  |  |  |
| 1 No | 47 (75.8%) | 46 (71.9%) | 253 (67.8%) | 144,534 (74.9%) |
| 2 Yes | 15 (24.2%) | 18 (28.1%) | 120 (32.2%) | 48,369 (25.1%) |
| **Alcohol drinking (times/week)** |  |  |  |  |
| 1 (>4 times) | 18 (29.0%) | 14 (21.9%) | 36 (9.7%) | 28,669 (14.9%) |
| 2 (4 times) | 10 (16.1%) | 8 (12.5%) | 63 (16.9%) | 34,184 (17.7%) |
| 3 (2-3 times) | 11 (17.7%) | 11 (17.2%) | 60 (16.1%) | 41,086 (21.3%) |
| 4 (1 time) | 5 (8.1%) | 2 (3.1%) | 23 (6.0%) | 17,599 (9.1%) |
| 5 (none) | 12 (19.4%) | 17 (26.5%) | 128 (34.3%) | 52,299 (27.1%) |
| *Missing* | 6 (9.7%) | 12 (18.8%) | 54 (16.0%) | 19,066 (9.9%) |
| **Metabolic syndrom**‡ |  |  |  |  |
| 1 No | 25 (40.3%) | 33 (51.5%) | 161 (43.2%) | 117,376 (60.9%) |
| 2 Yes | 37 (59.7%) | 31 (48.5%) | 212 (56.8%) | 75,686 (39.1%) |
| **Waist circumference** |  |  |  |  |
| 1 (women<80, men< 94 cm) | 12 (19.4%) | 24 (37.5%) | 114 (30.6%) | 85,266 (44.2%) |
| 2 (women ≥80, men ≥94 cm) | 50 (80.6%) | 40 (62.5%) | 259 (69.4%) | 107,637 (55.8%) |
| **High-density lipoprotein cholesterol (HDL)** | |  |  |  |
| 1 (women ≥1.3, men ≥1.0 mmol/L) | 52 (83.9%) | 52 (81.3%) | 279 (74.8%) | 145,286 (75.3%) |
| 2 (women<1.3, men<1.0 mmol/L) | 10 (16.1%) | 11 (17.2%) | 90 (24.1%) | 46,671 (24.2%) |
| **Triglycerides** |  |  |  |  |
| 1 (<1.7 mmol/L) | 29 (46.8%) | 43 (67.2%) | 211 (56.7%) | 121,012 (62.7%) |
| 2 (≥1.7 mmol/L) | 33 (53.2%) | 21 (32.8%) | 160 (42.9%) | 71,216 (36.9%) |
|  | 0 | 0 | 2 (0.4%) | 675 (0.4%) |
| **Hypertension**§ |  |  |  |  |
| 1 No | 17 (27.4%) | 13 (20.3%) | 78 (20.9%) | 86,243 (44.7%) |
| 2 Yes | 45 (72.6%) | 51 (79.7%) | 295 (79.1%) | 106,660 (55.3%) |
| **Non-fasting glucose** |  |  |  |  |
| 1 (<5.6 mmol/L) | 31 (50.0%) | 27 (42.2%) | 173 (46.4%) | 117,381 (60.9%) |
| 2 (≥5.6 mmol/L) | 31 (50.0%) | 37 (57.8%) | 200 (53.6%) | 75,522 (39.1%) |

† Standard deviation

‡ Metabolic syndrome was defined by the presence of ≥3 of following 5 factors: increased waist circumference (men≥94 cm, women≥80 cm), elevated triglycerides (≥1.7 mmol/L), low HDL (men<1.0 mmol/L, women<1.3 mmol/L), hypertension (systolic blood pressure ≥130 mm Hg, or diastolic blood pressure ≥85 mm Hg), and high non-fasting glucose (≥5.6 mmol/L).

§ Hypertension was defined with systolic blood pressure ≥130 mm Hg, or diastolic blood pressure ≥85 mm Hg.

**Table 2**. Hazard ratio (HR) with 95% confidence interval for incident esophageal adenocarcinoma and esophageal squamous-cell carcinoma related to metabolic syndrome.

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | **Esophageal adenocarcinoma** | | | **Esophageal squamous-cell carcinoma** | | |
| **Exposure** | **No.** | **HR†** | **HR‡** | **No.** | **HR†** | **HR§** |
|  |  |  |  |  |  |  |
| **Metabolic syndrome**# | |  |  |  |  |  |
| No | 25 | 1.0 | 1.0 | 33 | 1.0 | 1.0 |
| Yes | 37 | 1.54 (0.93-2.57) | 1.32 (0.77-2.26) | 31 | 0.98 (0.60-1.61) | 1.08 (0.64-1.83) |
|  |  |  |  |  |  |  |
| **Waist circumference** |  |  |  |  |  |  |
| Women<80 cm, men<94 cm | 12 | 1.0 | 1.0 | 24 | 1.0 | 1.0 |
| Women≥80 cm, men≥94 cm | 50 | 3.05 (1.62-5.75) | 2.48 (1.27-4.85) | 40 | 1.05 (0.63-1.75) | 1.19 (0.71-2.00) |
|  |  |  |  |  |  |  |
| **HDL** |  |  |  |  |  |  |
| Women≥1.3 mmol/L, men≥1.0 mmol/L | 52 | 1.0 | 1.0 | 52 | 1.0 | 1.0 |
| Women<1.3 mmol/L, men<1.0 mmol/L | 10 | 0.87 (0.44-1.72) | 0.76 (0.38-1.52) | 11 | 0.77 (0.40-1.49) | 0.70 (0.35-1.40) |
|  |  |  |  |  |  |  |
| **Triglycerides** |  |  |  |  |  |  |
| <1.7 mmol/L | 29 | 1.0 | 1.0 | 43 | 1.0 | 1.0 |
| ≥1.7 mmol/L | 33 | 1.35 (0.82-2.22) | 1.15 (0.69-1.91) | 21 | 0.65 (0.38-1.10) | 0.68 (0.40-1.15) |
|  |  |  |  |  |  |  |
| **Hypertension**¤ |  |  |  |  |  |  |
| No | 17 | 1.0 | 1.0 | 13 | 1.0 | 1.0 |
| Yes | 45 | 0.90 (0.51-1.60) | 0.82 (0.46-1.46) | 51 | 1.52 (0.80-2.88) | 1.62 (0.85-3.08) |
|  |  |  |  |  |  |  |
| **Non-fasting glucose^** |  |  |  |  |  |  |
| <5.6 mmol/L | 31 | 1.0 | 1.0 | 27 | 1.0 | 1.0 |
| ≥5.6 mmol/L | 31 | 1.09 (0.66-1.80) | 1.06 (0.63-1.78) | 37 | 1.63 (0.99-2.69) | 1.70 (1.00-2.90) |

† Adjusted for age (<60, ≥60 years), sex (women, men).

‡ Adjusted for age (<60, ≥60 years), sex (women, men), BMI (<25, 25-30, ≥ 30 kg/m2), education (primary/secondary school, high school, university), smoking status (no, yes); family cancer history (no, yes).

§ Adjusted for age (<60, ≥60 years), sex (women, men), BMI (<25, 25-30, ≥ 30 kg/m2), education (primary/secondary school, high school, university), smoking status (no, yes), alcohol intake (>4, 4, 2-3, 1 times per week, and none), family cancer history (no, yes).

# Metabolic syndrome was defined by the presence of ≥3 of following 5 factors: increased waist circumference (men≥94 cm, women≥80 cm), elevated triglycerides (≥1.7 mmol/L), low HDL (men<1.0 mmol/L, women<1.3 mmol/L), hypertension (systolic blood pressure ≥130 mm Hg, or diastolic blood pressure ≥85 mm Hg), and high non-fasting glucose (≥5.6 mmol/L).

^ Additionally adjusted for time since last meal (<3, 3-5, ≥5 hours).

**Table 3**. Hazard ratio (HR) with 95% confidence interval for incident gastric adenocarcinoma related to metabolic syndrome.

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Total** | | | **Women** | | | **Men** | | |
| **Exposure** | **No.** | **HR†** | **HR‡** | **No.** | **HR†** | **HR§** | **No.** | **HR†** | **HR§** |
|  |  |  |  |  |  |  |  |  |  |
| **Metabolic syndrome**# | | |  |  |  |  |  |  |  |
| No | 161 | 1.0 | 1.0 | 66 | 1.0 | 1.0 | 95 | 1.0 | 1.0 |
| Yes | 212 | 1.38 (1.12-1.70) | 1.44 (1.14-1.82) | 87 | 1.40 (1.00-1.95) | 1.64 (1.07-2.49) | 125 | 1.36 (1.04-1.78) | 1.36 (1.01-1.84) |
|  |  |  |  |  |  |  |  |  |  |
| **Waist circumference** | |  |  |  |  |  |  |  |  |
| Men<94 cm, women<80 cm | 114 | 1.0 | 1.0 | 40 | 1.0 | 1.0 | 74 | 1.0 | 1.0 |
| Men≥94 cm, women≥80 cm | 259 | 1.43 (1.14-1.79) | 1.47 (1.14-1.90) | 113 | 1.33 (0.92-1.92) | 1.71 (1.05-2.80) | 146 | 1.49 (1.12-1.97) | 1.38 (1.00-1.91) |
|  |  |  |  |  |  |  |  |  |  |
| **HDL** |  |  |  |  |  |  |  |  |  |
| Men≥1.0 mmol/L, women≥1.3 mmol/L | 279 | 1.0 | 1.0 | 111 | 1.0 | 1.0 | 168 | 1.0 | 1.0 |
| Men<1.0 mmol/L, women<1.3 mmol/L | 90 | 1.20 (0.94-1.54) | 1.18 (0.92-1.50) | 42 | 1.00 (0.70-1.42) | 1.02 (0.67-1.56) | 48 | 1.41 (1.02-1.95) | 1.34 (0.97-1.87) |
|  |  |  |  |  |  |  |  |  |  |
| **Triglycerides** | |  |  |  |  |  |  |  |  |
| <1.7 mmol/L | 211 | 1.0 | 1.0 | 95 | 1.0 | 1.0 | 116 | 1.0 | 1.0 |
| ≥1.7 mmol/L | 160 | 1.02 (0.83-1.26) | 0.99 (0.80-1.23) | 58 | 1.04 (0.74-1.46) | 1.00 (0.67-1.49) | 102 | 1.00 (0.77-1.31) | 0.95 (0.72-1.25) |
|  |  |  |  |  |  |  |  |  |  |
| **Hypertension**¤ | |  |  |  |  |  |  |  |  |
| No | 78 | 1.0 | 1.0 | 32 | 1.0 | 1.0 | 46 | 1.0 | 1.0 |
| Yes | 295 | 1.54 (1.19-2.01) | 1.52 (1.16-1.98) | 121 | 2.09 (1.35-3.22) | 2.41 (1.44-4.03) | 174 | 1.27 (0.91-1.77) | 1.24 (0.88-1.73) |
|  |  |  |  |  |  |  |  |  |  |
| **Non-fasting glucose^** | |  |  |  |  |  |  |  |  |
| <5.6 mmol/L | 173 | 1.0 | 1.0 | 69 | 1.0 | 1.0 | 104 | 1.0 | 1.0 |
| ≥5.6 mmol/L | 200 | 1.33 (1.08-1.63) | 1.36 (1.10-1.69) | 84 | 1.56 (1.13-2.15) | 1.74 (1.18-2.56) | 116 | 1.19 (0.91-1.55) | 1.22 (0.92-1.62) |

† Adjusted for age (<60, ≥60 years).

‡ Adjusted for age (<60, ≥60 years), sex (women, men), BMI (<25, 25-30,≥ 30 kg/m2 ), education (primary/secondary school, high school, university), smoking status (no, yes); family cancer history (no, yes).

§ Adjusted for age (<60, ≥60 years), BMI (<25, 25-30,≥ 30 kg/m2 ), education (primary/secondary school, high school, university), smoking status (no, yes); family cancer history (no, yes).

# Metabolic syndrome was defined by the presence of ≥3 of following 5 factors: increased waist circumference (men≥94 cm, women≥80 cm), elevated triglycerides (≥1.7 mmol/L), low HDL (men<1.0 mmol/L, women<1.3 mmol/L), hypertension (systolic blood pressure ≥130 mm Hg, or diastolic blood pressure ≥85 mm Hg), and high non-fasting glucose (≥5.6 mmol/L).

^ Additionally adjusted for time since last meal (<3, 3-5, ≥5 hours).