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| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Appendix Table 1. Hazard ratios for cancer incidence for different serum iron levels by smoking status** | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| **Serum iron (μg/dL)** |  | **<60** | | | | |  | **60-79** | |  |  | **80-99** | | | | |  | **100-119** | | | | |  | **≧120** | | | | |  | **≧140** | | | | |
|  | Total | case | HR |  | 95%CI | |  | case | HR |  |  | case | HR |  | 95%CI | |  | case | HR |  | 95%CI | |  | case | HR |  | 95%CI | |  | case | HR |  | 95%CI | |
| **Total** | 8060 | 1302 | 1.18 | \* | (1.08, | 1.29) |  | 1469 | 1.00 |  |  | 1752 | 1.01 |  | (0.94, | 1.09) |  | 1456 | 1.06 |  | (0.97, | 1.15) |  | 2081 | 1.25 | \* | (1.16, | 1.35) |  | 1118 | 1.37 | \* | (1.26, | 1.50) |
| Smoker | 2771 | 353 | 1.40 | \* | (1.20, | 1.65) |  | 376 | 1.00 |  |  | 534 | 1.07 |  | (0.93, | 1.24) |  | 504 | 1.15 |  | (0.99, | 1.32) |  | 1004 | 1.43 | \* | (1.26, | 1.63) |  | 585 | 1.53 | \* | (1.33, | 1.77) |
| Nonsmoker | 5289 | 949 | 1.10 |  | (0.99, | 1.22) |  | 1093 | 1.00 |  |  | 1218 | 0.99 |  | (0.91, | 1.09) |  | 952 | 1.03 |  | (0.93, | 1.14) |  | 1077 | 1.17 | \* | (1.06, | 1.29) |  | 533 | 1.29 | \* | (1.15, | 1.46) |
|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| **Male** | 4177 | 507 | 1.39 | \* | (1.21, | 1.59) |  | 594 | 1.00 |  |  | 858 | 1.08 |  | (0.96, | 1.21) |  | 796 | 1.13 | \* | (1.01, | 1.28) |  | 1422 | 1.36 | \* | (1.22, | 1.52) |  | 812 | 1.46 | \* | (1.30, | 1.65) |
| Smoker | 2520 | 306 | 1.51 | \* | (1.27, | 1.79) |  | 324 | 1.00 |  |  | 482 | 1.11 |  | (0.95, | 1.29) |  | 462 | 1.20 |  | (1.03, | 1.39) |  | 946 | 1.49 | \* | (1.30, | 1.71) |  | 552 | 1.59 | \* | (1.37, | 1.84) |
| Nonsmoker | 1657 | 201 | 1.27 | \* | (1.01, | 1.58) |  | 270 | 1.00 |  |  | 376 | 1.05 |  | (0.87, | 1.26) |  | 334 | 1.07 |  | (0.89, | 1.28) |  | 476 | 1.22 | \* | (1.02, | 1.45) |  | 260 | 1.31 | \* | (1.07, | 1.61) |
|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| **Female** | 3883 | 795 | 1.03 |  | (0.92, | 1.16) |  | 875 | 1.00 |  |  | 894 | 0.97 |  | (0.87, | 1.08) |  | 660 | 1.00 |  | (0.90, | 1.13) |  | 659 | 1.15 | \* | (1.03, | 1.29) |  | 306 | 1.32 | \* | (1.14, | 1.52) |
| Smoker | 251 | 47 | 0.93 |  | (0.61, | 1.41) |  | 52 | 1.00 |  |  | 52 | 0.89 |  | (0.59, | 1.32) |  | 42 | 0.86 |  | (0.56, | 1.32) |  | 58 | 1.14 |  | (0.77, | 1.69) |  | 33 | 1.30 |  | (0.82, | 2.05) |
| Nonsmoker | 3632 | 748 | 1.05 |  | (0.93, | 1.18) |  | 823 | 1.00 |  |  | 842 | 0.98 |  | (0.88, | 1.09) |  | 618 | 1.02 |  | (0.90, | 1.14) |  | 601 | 1.15 | \* | (1.02, | 1.29) |  | 273 | 1.30 | \* | (1.12, | 1.52) |
| Reference group: serum iron level at 60-79 μg/dL.  Adjusted for age, gender, BMI, systolic blood pressure, total cholesterol, C-reactive protein, hemoglobin, smoking, drinking, and physical activity in a multivariate Cox model. \*Indicates a significantly (p<0.05) higher incidence compared to 60-79 μg/dL serum iron group. | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
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|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Appendix Table 2. Cancer mortality risk for different serum iron levels** | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| **Serum iron (μg/dL)** | | **<60** | | | | |  | **60-79** | |  | **80-99** | | | | |  | **100-119** | | | | |  | **≧120** | | | | |  | **≧140** | | | | |  |  | |
|  | Total | cases | HR |  | 95% CI | |  | cases | HR |  | cases | HR |  | 95% CI | |  | cases | HR |  | 95% CI | |  | cases | HR |  | 95% CI | |  | cases | HR |  | 95% CI | |  | *p for trend* | |
| **Total** |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | |
| All cancer | 3066 | 525 | 1.30 | \* | (1.13, | 1.49) |  | 521 | 1.00 |  | 627 | 1.04 |  | (0.91, | 1.18) |  | 554 | 1.13 |  | (0.99, | 1.29) |  | 839 | 1.39 | \* | (1.23, | 1.57) |  | 486 | 1.62 | \* | (1.41, | 1.86) |  | ＜0.0001 | |
| Liver | 606 | 82 | 1.76 | \* | (1.22, | 2.55) |  | 64 | 1.00 |  | 84 | 1.20 |  | (0.84, | 1.71) |  | 120 | 1.79 | \* | (1.27, | 2.51) |  | 256 | 2.86 | \* | (2.10, | 3.90) |  | 167 | 3.54 | \* | (2.56, | 4.91) |  | ＜0.0001 | |
| Lung | 674 | 98 | 1.06 |  | (0.79, | 1.42) |  | 130 | 1.00 |  | 161 | 1.07 |  | (0.83, | 1.37) |  | 122 | 1.01 |  | (0.78, | 1.32) |  | 163 | 1.00 |  | (0.77, | 1.29) |  | 83 | 1.04 |  | (0.77, | 1.41) |  |  | |
| Colorectal | 300 | 85 | 2.21 | \* | (1.52, | 3.20) |  | 51 | 1.00 |  | 69 | 0.99 |  | (0.68, | 1.45) |  | 51 | 1.01 |  | (0.68, | 1.51) |  | 44 | 0.71 |  | (0.46, | 1.08) |  | 23 | 0.80 |  | (0.48, | 1.34) |  |  | |
| **Male** |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | |  |
| All cancer | 1914 | 282 | 1.43 | \* | (1.19, | 1.74) |  | 275 | 1.00 |  | 363 | 1.02 |  | (0.86, | 1.21) |  | 354 | 1.09 |  | (0.92, | 1.30) |  | 640 | 1.38 | \* | (1.18, | 1.61) |  | 396 | 1.60 | \* | (1.35, | 1.90) |  | ＜0.0001 | |
| Liver | 465 | 57 | 2.13 | \* | (1.34, | 3.38) |  | 43 | 1.00 |  | 55 | 1.10 |  | (0.70, | 1.72) |  | 89 | 1.71 | \* | (1.12, | 2.59) |  | 221 | 2.57 | \* | (1.76, | 3.76) |  | 139 | 3.03 | \* | (2.05, | 4.50) |  | ＜0.0001 | |
| Lung | 448 | 54 | 1.16 |  | (0.78, | 1.72) |  | 70 | 1.00 |  | 111 | 1.22 |  | (0.88, | 1.69) |  | 80 | 1.01 |  | (0.71, | 1.42) |  | 133 | 1.08 |  | (0.79, | 1.48) |  | 73 | 1.13 |  | (0.79, | 1.61) |  |  | |
| Colorectal | 187 | 48 | 2.30 | \* | (1.40, | 3.76) |  | 30 | 1.00 |  | 40 | 0.87 |  | (0.53, | 1.43) |  | 34 | 0.89 |  | (0.53, | 1.47) |  | 35 | 0.68 |  | (0.41, | 1.13) |  | 20 | 0.77 |  | (0.43, | 1.39) |  |  | |
| Prostate | 61 | 8 | 0.81 |  | (0.33, | 1.94) |  | 17 | 1.00 |  | 14 | 0.56 |  | (0.27, | 1.16) |  | 12 | 0.59 |  | (0.28, | 1.24) |  | 10 | 0.34 |  | (0.15, | 0.78) |  | 8 | 0.54 |  | (0.22, | 1.33) |  |  | |
| **Female** |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | |
| All cancer | 1152 | 243 | 1.17 |  | (0.95, | 1.43) |  | 246 | 1.00 |  | 264 | 1.07 |  | (0.89, | 1.30) |  | 200 | 1.22 |  | (0.99, | 1.50) |  | 199 | 1.38 | \* | (1.11, | 1.70) |  | 90 | 1.57 | \* | (1.20, | 2.06) |  | 0.0003 | |
| Liver | 170 | 28 | 1.33 |  | (0.71, | 2.49) |  | 23 | 1.00 |  | 34 | 1.42 |  | (0.79, | 2.55) |  | 32 | 1.91 | \* | (1.05, | 3.45) |  | 53 | 3.97 | \* | (2.30, | 6.83) |  | 35 | 6.20 | \* | (3.44, | 11.17) |  | ＜0.0001 | |
| Lung | 226 | 44 | 0.93 |  | (0.59, | 1.45) |  | 60 | 1.00 |  | 50 | 0.85 |  | (0.57, | 1.27) |  | 42 | 1.10 |  | (0.72, | 1.68) |  | 30 | 0.84 |  | (0.51, | 1.38) |  | 10 | 0.80 |  | (0.39, | 1.65) |  |  | |
| Breast | 97 | 17 | 0.81 |  | (0.40, | 1.66) |  | 21 | 1.00 |  | 20 | 0.89 |  | (0.47, | 1.69) |  | 16 | 0.89 |  | (0.44, | 1.81) |  | 23 | 1.56 |  | (0.83, | 2.93) |  | 10 | 1.75 |  | (0.81, | 3.81) |  | 0.0999 | |
| Colorectal | 113 | 37 | 2.09 | \* | (1.18, | 3.68) |  | 21 | 1.00 |  | 29 | 1.20 |  | (0.67, | 2.17) |  | 17 | 1.25 |  | (0.65, | 2.38) |  | 9 | 0.65 |  | (0.28, | 1.56) |  | 3 | 0.73 |  | (0.21, | 2.47) |  |  | |
| HR was adjusted for age, BMI, systolic blood pressure, total cholesterol, C-reactive protein, hemoglobin, smoking, drinking, and physical activity.  HR for liver cancer was additionally adjusted for HBV among subjects without liver cirrhosis and HCV(+).  \*Indicates a significantly (p<0.05) higher incidence compared to the group with 60-79 μg/dL serum iron. | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |

**Appendix Table 3. Comparison of results of first and second test of serum iron**

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Serum iron (ug/dL)** | | **<60** | |  | **60-79** | | | | | |  | **80-99** | |  | **100-119** | |  | **≧120** | | | | | | |
|  | Total | n | % |  | n | % | Cases | HRs | 95%CI | |  | n | % |  | n | % |  | n | % | Cases | HRs |  | 95%CI | |
| **Male** |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| 1st | 60686 | 4410 | 7.3% |  | 8940 | 14.7% | 255 | 1.00 | - | |  | 13113 | 21.6% |  | 12968 | 21.4% |  | 21255 | 35.0% | 616 | 1.35 | \* | (1.15 | ,1.58) |
| 2nd | 60686 | 4466 | 7.4% |  | 9509 | 15.7% | 294 | 1.00 | - | |  | 13275 | 21.9% |  | 12728 | 21.0% |  | 20708 | 34.1% | 591 | 1.22 | \* | (1.05 | ,1.43) |
| **Female** | |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| 1st | 68875 | 14604 | 21.2% |  | 14362 | 20.9% | 428 | 1.00 | - | |  | 15397 | 22.4% |  | 11832 | 17.2% |  | 12680 | 18.4% | 324 | 1.10 |  | (0.94 | ,1.30) |
| 2nd | 68875 | 14735 | 21.4% |  | 14434 | 21.0% | 409 | 1.00 | - | |  | 15634 | 22.7% |  | 11740 | 17.0% |  | 12332 | 17.9% | 332 | 1.13 |  | (0.96 | ,1.33) |
| **All** |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| 1st | 129561 | 19014 | 14.7% |  | 23302 | 18.0% | 683 | 1.00 | - | |  | 28510 | 22.0% |  | 24800 | 19.1% |  | 33935 | 26.2% | 940 | 1.25 | \* | (1.16 | ,1.35) |
| 2nd | 129561 | 19201 | 14.8% |  | 23943 | 18.5% | 703 | 1.00 | - | |  | 28909 | 22.3% |  | 24468 | 18.9% |  | 33040 | 25.5% | 923 | 1.22 | \* | (1.09 | ,1.36) |

HRs: Hazard ratios for all cancer incidence are adjusted for age and gender when appropriate.

\*p<0.05

**Appendix Figure 1. J-shaped relationship between serum iron and cancer risk**

Spline figure Appendix figure 1 .tif

Spline regression was applied to modeling the continuous serum iron and cancer risk (knot at serum=80 μg/dL and degree=3). \*p<0.05.