**Table A. Standardized incidence ratios for specific cancer types among patients with breast cancer (including subsequent malignancy occurred within one year)**

|  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | Total |  |  |  | Male |  |  |  | Female |  |  |
| Site of cancers | Observed | Expected | SIR (95% CI) |  | Observed | Expected | SIR (95% CI) |  | Observed | Expected | SIR (95% CI) |
| All cancers | 3,153 | 2,090.51 | 1.51(1.46–1.56) |  | 73 | 33.63 | 2.17(1.70–2.73) |  | 3,080 | 2,056.89 | 1.50(1.44–1.55) |
| Head and neck | 99 | 86.05 | 1.15(0.94–1.40) |  | 13 | 2.95 | 4.41(2.35–7.54) |  | 86 | 83.10 | 1.03(0.83–1.28) |
| Digestive | 1121 | 862.58 | 1.30(1.22–1.38) |  | 23 | 14.91 | 1.54(0.98–2.31) |  | 1,098 | 847.67 | 1.30(1.22–1.37) |
| Esophagus | 12 | 11.22 | 1.07(0.55–1.87) |  | 0 | 0.92 | 0.00(0.00–4.00) |  | 12 | 10.30 | 1.17(0.60–2.04) |
| Stomach | 151 | 110.49 | 1.37(1.16–1.60) |  | 4 | 2.39 | 1.67(0.46–4.28) |  | 147 | 108.10 | 1.36(1.15–1.60) |
| Colon and rectum, Anus | 555 | 403.65 | 1.37(1.26–1.49) |  | 12 | 5.51 | 2.18(1.13–3.80) |  | 543 | 398.15 | 1.36(1.25–1.48) |
| Liver and biliary tract | 340 | 289.65 | 1.17(1.05–1.31) |  | 6 | 5.41 | 1.11(0.41–2.41) |  | 334 | 284.24 | 1.18(1.05–1.31) |
| Pancreas | 63 | 47.56 | 1.32(1.02–1.69) |  | 1 | 0.68 | 1.48(0.04–8.24) |  | 62 | 46.89 | 1.32(1.01–1.70) |
| Lung and mediastinum | 426 | 279.31 | 1.53(1.38–1.68) |  | 11 | 5.85 | 1.88(0.94–3.36) |  | 415 | 273.46 | 1.52(1.38–1.67) |
| Bone and Soft tissue | 43 | 20.16 | 2.13(1.54–2.87) |  | 0 | 0.25 | 0.00(0.00–14.83) |  | 43 | 19.91 | 2.16(1.56–2.91) |
| Skin | 58 | 52.10 | 1.11(0.85–1.44) |  | 6 | 0.73 | 8.24(3.02–17.94) |  | 52 | 51.37 | 1.01(0.76–1.33) |
| Genitourinary | 849 | 521.60 | 1.63(1.52–1.74) |  | 12 | 6.79 | 1.77(0.91–3.09) |  | 837 | 514.81 | 1.63(1.52–1.74) |
| Cervix | 159 | 186.29 | 0.85(0.73–1.00) |  | N/A | N/A | N/A |  | 159 | 186.29 | 0.85(0.73–1.00) |
| Uterus | 298 | 111.94 | 2.66(2.37–2.98) |  | N/A | N/A | N/A |  | 298 | 111.94 | 2.66(2.37–2.98) |
| Ovary | 171 | 83.60 | 2.05(1.75–2.38) |  | N/A | N/A | N/A |  | 171 | 83.60 | 2.05(1.75–2.38) |
| Prostate | 8 | 4.26 | 1.88(0.81–3.70) |  | 8 | 4.26 | 1.88(0.81–3.70) |  | N/A | N/A | N/A |
| Bladder | 72 | 59.62 | 1.21(0.94–1.52) |  | 3 | 1.70 | 1.76(0.36–5.15) |  | 69 | 57.92 | 1.19(0.93–1.51) |
| Kidney | 141 | 75.88 | 1.86(1.56–2.19) |  | 1 | 0.83 | 1.21(0.03–6.74) |  | 140 | 75.06 | 1.87(1.57–2.20) |
| Thyroid | 238 | 102.56 | 2.32(2.04–2.64) |  | 2 | 0.15 | 13.20(1.60–47.69) |  | 236 | 102.40 | 2.30(2.02–2.62) |
| Hematologic malignancies | 192 | 112.06 | 1.71(1.48–1.97) |  | 4 | 1.51 | 2.66(0.72–6.80) |  | 188 | 110.56 | 1.70(1.47–1.96) |
| All Others | 127 | 54.10 | 2.35(1.96–2.79) |  | 2 | 0.49 | 4.06(0.49–14.67) |  | 125 | 53.61 | 2.33(1.94–2.78) |

SIR Standardized incidence ratio; CI confidence interval; N/A not applicable.

**Table B. Risk factors for uterine cancer development in patients with breast cancer**

**Multivariable analysis: *p*<0.1 enter**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | Univariate analysis | |  | Multivariateanalysisa | |
| Variables | HR (95% CI) | *P* Value |  | HR (95% CI) | *P* Value |
| Age increases per 10 years | 1.28 (1.16–1.40) | < 0.001 |  | 1.26 (1.15–1.38) | < 0.001 |
| **Comorbidities** |  |  |  |  |  |
| Diabetes mellitus | 1.11 (0.80–1.54) | 0.530 |  |  |  |
| COPD | 1.13 (0.80–1.61) | 0.482 |  |  |  |
| Chronic kidney disease | 0.97 (0.59–1.61) | 0.908 |  |  |  |
| Liver cirrhosis | 0.41 (0.06–2.88) | 0.367 |  |  |  |
| Autoimmune diseases | 1.42 (0.92–2.20) | 0.115 |  |  |  |
| Dyslipidemia | 1.04 (0.76–1.42) | 0.809 |  |  |  |
| **Breast Cancer Treatmentb** | |  |  |  |  |
| Hormone treatment |  |  |  |  |  |
| Anastrozole | 1.50 (1.08–2.09) | 0.016 |  | 1.29 (0.93–1.80) | 0.130 |
| Letrozole | 1.09 (0.72–1.65) | 0.675 |  |  |  |
| Exemestane | 0.55 (0.24–1.23) | 0.145 |  |  |  |
| Tamoxifen | 1.85 (1.38–2.49) | < 0.001 |  | 1.79 (1.33–2.40) | < 0.001 |
| Chemotherapy | 1.03 (0.81–1.31) | 0.833 |  |  |  |
| Trastuzumab | 0.87 (0.36–2.11) | 0.757 |  |  |  |
| Radiotherapy | 0.91 (0.71–1.16) | 0.438 |  |  |  |

Abbreviation: COPD = Chronic obstructive pulmonary disease; ESRD = End-stage renal disease

aAll factors with *p*< 0.1 in univariate analyses were included in the Cox multivariate analysis.

bTreatment as time-dependent covariate in Cox model

**Table C. Risk factors for lung cancers development in patients with breast cancer**

**Multivariable analysis: *p*<0.1 enter**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | Univariate analysis | |  | Multivariateanalysisa | |
| Variables | HR (95% CI) | *P* Value |  | HR (95% CI) | *P* Value |
| Age increases per 10 years | 1.54 (1.43–1.66) | < 0.001 |  | 1.50 (1.38–1.63) | < 0.001 |
| Gender (male) | 5.05 (2.77–9.18) | < 0.001 |  | 3.02 (1.64–5.54) | < 0.001 |
| **Comorbidities** |  |  |  |  |  |
| Diabetes mellitus | 1.43 (1.12–1.83) | 0.005 |  | 0.83 (0.63–1.09) | 0.185 |
| COPD | 1.96 (1.54–2.49) | < 0.001 |  | 1.37 (1.07–1.76) | 0.014 |
| Chronic kidney disease | 0.95 (0.63–1.44) | 0.824 |  |  |  |
| Liver cirrhosis | 1.61 (0.72–3.62) | 0.245 |  |  |  |
| Autoimmune diseases | 1.91 (1.39–2.61) | < 0.001 |  | 1.47 (1.07–2.03) | 0.018 |
| Dyslipidemia | 1.85 (1.49–2.30) | < 0.001 |  | 1.30 (1.02–1.65) | 0.037 |
| **Breast Cancer Treatment** | |  |  |  |  |
| Hormone treatment | 0.77 (0.63–0.95) | 0.014 |  | 0.72 (0.59–0.88) | 0.002 |
| Chemotherapy | 0.80 (0.66–0.97) | 0.025 |  | 1.09 (0.89–1.35) | 0.397 |
| Trastuzumab | 0.85 (0.40–1.79) | 0.662 |  |  |  |
| Radiotherapy | 1.04 (0.85–1.28) | 0.687 |  |  |  |

Abbreviation: COPD = Chronic obstructive pulmonary disease; ESRD = End-stage renal disease

aAll factors with *p*< 0.1 in univariate analyses were included in the Cox multivariate analysis.

**Table D. Risk factors for liver cancers development in patients with breast cancer**

**Multivariable analysis: *p*<0.1 enter**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | Univariate analysis | |  | Multivariateanalysisa | |
| Variables | HR (95% CI) | *P* Value |  | HR (95% CI) | *P* Value |
| Age increases per 10 years | 1.91 (1.76–2.07) | < 0.001 |  | 1.84 (1.67–2.03) | < 0.001 |
| Gender (male) | 3.47 (1.55–7.79) | 0.003 |  | 1.69 (0.75–3.81) | 0.207 |
| **Comorbidities** |  |  |  |  |  |
| Diabetes mellitus | 3.18 (2.52–4.01) | < 0.001 |  | 1.62 (1.24–2.10) | < 0.001 |
| COPD | 1.61 (1.20–2.15) | 0.001 |  | 0.79 (0.58–1.07) | 0.121 |
| Chronic kidney disease | 2.52 (1.83–3.47) | < 0.001 |  | 1.37 (0.98–1.92) | 0.068 |
| Liver cirrhosis | 25.27 (19.03–33.55) | < 0.001 |  | 16.63 (12.38–22.35) | < 0.001 |
| Autoimmune diseases | 1.50 (1.01–2.23) | 0.045 |  | 0.96 (0.64–1.44) | 0.843 |
| Dyslipidemia | 1.97 (1.54–2.52) | < 0.001 |  | 0.92 (0.70–1.21) | 0.537 |
| **Breast Cancer Treatment** | |  |  |  |  |
| Hormone treatment | 1.02 (0.80–1.30) | 0.894 |  |  |  |
| Chemotherapy | 0.82 (0.66–1.02) | 0.075 |  | 1.50 (1.18–1.91) | 0.001 |
| Trastuzumab | 1.02 (0.48–2.16) | 0.953 |  |  |  |
| Radiotherapy | 0.67 (0.53–0.85) | 0.001 |  | 0.87 (0.68–1.11) | 0.267 |

Abbreviation: COPD = Chronic obstructive pulmonary disease; ESRD = End-stage renal disease

aAll factors with *p*< 0.1 in univariate analyses were included in the Cox multivariate analysis.