

Renal Outcome in Patients with Urothelial Carcinoma in Taiwan: A 12-year Population-based Observational Study

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OBJECTIVES

Previous literature suggested an increased risk of urothelial carcinoma (UC) in patients with end-stage renal disease (ESRD). However, the association between UC and subsequent ESRD incidence has not been confirmed.

METHODS

We construct a population-based retrospective cohort study to examine the risk of ESRD in UC patients in Taiwan. The study cohort consists of 26,017 patients newly diagnosed with UC, but without prior history of ESRD, derived from the National Health Institutes claims data from 1998 to 2010, together with 208,136 matched enrollees as a comparison cohort. The incidence of ESRD was ascertained through cross-referencing with the registry of catastrophic illnesses. Cox proportional hazard regression and Kaplan–Meier analyses were conducted to compute the ESRD-free survival rates after adjusting for possible confounding factors.

RESULTS

Of 234,153 study participants, 979 (3.76%) from the UC group and 1,829 (0.88%) from the comparison group had a subsequent diagnosis of ESRD during the follow-up period. Compared with the control group, the hazard ratios were 7.75 [95% confidence interval (CI): 6.84 to 8.78] and 3.12 (95% CI: 6.84 to 8.78) after adjusting for potential confounders in the upper urinary tract UC (UT-UC) and bladder UC (B-UC), respectively. Women either with UT-UC or B-UC both had higher risks of ESRD than men.

Table 1 Demographic characteristics and comorbidities of the UC and control groups in Taiwan

| Variable | Control group | UC group | UT-UC group | B-UC group | p |
|----------------------------|---------------|--------------|-------------|--------------|---------|
| Total number | 208136 | 26017 | 4263 | 21537 | |
| Follow-up year (mean ± SD) | 4.79 ± 3.43 | 3.80 ± 3.27 | 2.94 ± 2.81 | 3.98 ± 3.33 | <0.001 |
| Gender | | | | | 1.00 |
| Male | 145176 (69.7) | 18147 (69.7) | 1857 (43.6) | 16176 (75.1) | |
| Female | 62960 (30.3) | 7870 (30.3) | 2406 (56.4) | 5361 (24.9) | |
| Age, year | | | | | 1.00 |
| 25-44 | 9496 (4.56) | 1187 (4.56) | 130 (3.05) | 1036 (4.81) | |
| 45-54 | 23688 (11.4) | 2961 (11.4) | 396 (9.29) | 2537 (11.8) | |
| 55-64 | 40504 (19.5) | 5063 (19.5) | 878 (20.6) | 4151 (19.3) | |
| 65-74 | 66096 (31.8) | 8262 (31.8) | 1596 (37.4) | 6591 (30.6) | |
| ≥75 | 68352 (32.8) | 8544 (32.8) | 1263 (29.6) | 7222 (33.5) | |
| Geographic region | | | | | <0.0001 |
| Northern | 86554 (41.6) | 8970 (34.5) | 861 (20.2) | 8047 (37.4) | |
| Central | 42928 (20.6) | 4888 (18.8) | 819 (19.2) | 4039 (18.8) | |
| Southern | 57490 (27.6) | 9601 (36.9) | 2139 (50.2) | 7360 (34.2) | |
| Eastern | 21159 (10.2) | 2558 (9.83) | 444 (10.4) | 2091 (9.71) | |
| Occupation | | | | | <0.0001 |
| White collar | 88544 (42.6) | 11240 (43.2) | 1757 (41.2) | 9396 (43.6) | |
| Blue collar | 86942 (41.9) | 11563 (44.5) | 2224 (52.2) | 9232 (42.9) | |
| Others | 32237 (15.5) | 3208 (12.3) | 281 (6.59) | 2904 (13.5) | |
| Monthly income, NTD | | | | | <0.0001 |
| ≤ 15840 | 118082 (56.7) | 14832 (57.0) | 2149 (50.4) | 12569 (58.4) | |
| 15841–20100 | 9569 (4.60) | 2116 (8.13) | 387 (9.08) | 1700 (7.89) | |
| > 20100 | 80485 (38.7) | 9069 (34.9) | 1727 (40.5) | 7268 (33.8) | |
| Diabetes | 18522 (8.90) | 4493 (17.3) | 900 (21.1) | 3557 (16.5) | <0.0001 |
| Hypertension | 36179 (17.4) | 8635 (33.2) | 1753 (41.1) | 6808 (31.6) | <0.0001 |
| Coronary heart disease | 18544 (8.91) | 2988 (11.5) | 546 (12.8) | 2416 (11.2) | <0.0001 |
| Atrial fibrillation | 3796 (1.82) | 537 (2.06) | 83 (1.95) | 452 (2.10) | 0.007 |
| Heart failure | 5854 (2.81) | 880 (3.38) | 168 (3.94) | 702 (3.26) | <0.0001 |
| Chronic kidney disease | 1266 (0.61) | 560 (2.16) | 157 (3.68) | 400 (1.86) | <0.0001 |
| Hyperlipidemia | 8119 (3.90) | 1371 (5.27) | 280 (6.57) | 1077 (5.00) | <0.0001 |
| Nephroureterectomy | 405 (0.19) | 4854 (18.7) | 3306 (77.6) | 1508 (7.00) | <0.0001 |

Table 3 Multivariate Cox proportional hazards model for the prediction of ESRD¹

| | ESRD number | Person-years | Rate, per 1,000 person-years | Age, sex-adjusted HRs (95% CI) | Multivariate-HRs (95% CI) |
|----------------------------|-------------|--------------|------------------------------|--------------------------------|---------------------------|
| Control | 1829 | 997339 | | 1.83 | 1 |
| UC (Total) | | | | | |
| Without Nephroureterectomy | 553 | 82887 | | 6.67 3.72 (3.38–4.09)*** | 2.74 (2.48–3.01)*** |
| With Nephroureterectomy | 426 | 16042 | | 26.56 13.8 (12.4–15.4)*** | 8.88 (7.95–9.93)*** |
| UT-UC | | | | | |
| Without Nephroureterectomy | 73 | 2221 | | 32.87 16.6 (13.1–21.0)*** | 7.07 (5.55–9.01)*** |
| With Nephroureterectomy | 257 | 10294 | | 24.97 13.0 (11.4–14.8)*** | 8.25 (7.20–9.45)*** |
| Bladder UC | | | | | |
| Without Nephroureterectomy | 475 | 80137 | | 5.93 3.31 (2.99–3.66)*** | 2.50 (2.26–2.77)*** |
| With Nephroureterectomy | 167 | 5613 | | 29.75 15.9 (13.6–18.6)*** | 10.6 (8.99–12.4)*** |

¹ Multivariate model adjusted for age, sex, geographic region, occupation, monthly income, and comorbidities (including diabetes, hypertension, coronary heart disease, atrial fibrillation, heart failure, chronic kidney disease, and hyperlipidemia).

Table 2 Multivariate Cox proportional hazards model for the prediction of ESRD¹

| | ESRD number | Person-years | Rate, per 1,000 person-years | Age, sex-adjusted HRs (95% CI) | Multivariate-HRs (95% CI) |
|------------|-------------|--------------|------------------------------|--------------------------------|---------------------------|
| All | | | | | |
| Control | 1829 | 997339 | | 1.83 | 1 |
| UC (Total) | 979 | 98929 | | 9.9 5.46 (5.05–5.91) | 3.87 (3.57–4.19) |
| UT-UC | 330 | 12515 | | 16.37 13.5 (11.9–15.2)*** | 7.75 (6.84–8.78)*** |
| Bladder UC | 642 | 85750 | | 7.49 4.18 (3.82–4.57)*** | 3.12 (2.84–3.42)*** |
| Male | | | | | |
| Control | 1239 | 695972 | | 1.78 | 1 |
| UC (Total) | 515 | 71278 | | 7.23 4.05 (3.66–4.49)*** | 2.93 (2.63–3.25)*** |
| UT-UC | 102 | 5410 | | 18.85 10.8 (8.81–13.2)*** | 6.16 (5.00–7.57)*** |
| Bladder UC | 410 | 65551 | | 6.25 3.50 (3.13–3.92)*** | 2.60 (2.32–2.91)*** |
| Female | | | | | |
| Control | 590 | 301367 | | 1.96 | 1 |
| UC (Total) | 464 | 27651 | | 16.78 8.69 (7.69–9.82)*** | 5.98 (5.26–6.80)*** |
| UT-UC | 228 | 7105 | | 32.09 16.5 (14.2–19.3)*** | 9.87 (8.37–11.6)*** |
| Bladder UC | 232 | 20199 | | 11.49 5.99 (5.14–6.97)*** | 4.45 (3.81–5.21)** |

¹ Multivariate model adjusted for age, sex, geographic region, occupation, monthly income, and comorbidities (including diabetes, hypertension, coronary heart disease, atrial fibrillation, heart failure, chronic kidney disease, and hyperlipidemia).

Table 4 Interaction between clinical comorbidities and different UC type in ESRD¹

| | Multivariate-HRs (95% CI) | P for interaction | | Multivariate-HRs (95% CI) | P for interaction | | Multivariate-HRs (95% CI) | P for interaction |
|-----------|---------------------------|-------------------|----------|---------------------------|-------------------|----------|---------------------------|-------------------|
| CKD UC | 0.3 | | DM UC | <0.0001 | | HT UC | <0.0001 | |
| No No | 1 | | No No | 1 | | No No | 1 | |
| Yes Yes | 3.93 (3.61–4.29)*** | | Yes Yes | 5.28 (4.80–5.81)*** | | Yes Yes | 5.20 (4.70–5.76)*** | |
| Yes No | 16.5 (14.0–19.4)*** | | Yes No | 4.73 (4.24–5.27)*** | | Yes No | 2.33 (2.09–2.60)*** | |
| No Yes | 57.6 (48.9–67.8)*** | | No Yes | 10.1 (8.84–11.6)*** | | No Yes | 5.98 (5.26–6.80)*** | |
| CKD UT-UC | 0.0003 | | DM UT-UC | <0.0001 | | HT UT-UC | <0.0001 | |
| No No | 1 | | No No | 1 | | No No | 1 | |
| Yes Yes | 8.99 (7.84–10.3)*** | | Yes Yes | 12.0 (10.4–14.0)*** | | Yes Yes | 12.0 (10.2–14.1) | |
| Yes No | 14.5 (12.3–17.1)*** | | Yes No | 4.68 (4.18–5.24)*** | | Yes No | 2.20 (1.95–2.47)*** | |
| No Yes | 71.5 (54.7–93.5)*** | | No Yes | 20.9 (16.9–25.8)*** | | No Yes | 11.8 (9.77–14.3)*** | |
| CKD B-UC | 0.59 | | DM B-UC | <0.0001 | | HT B-UC | <0.0001 | |
| No No | 1 | | No No | 1 | | No No | 1 | |
| Yes Yes | 3.01 (2.73–3.33)*** | | Yes Yes | 4.18 (3.75–4.67)*** | | Yes Yes | 4.12 (3.67–4.63)*** | |
| Yes No | 15.7 (13.3–18.4)*** | | Yes No | 4.64 (4.15–5.18)*** | | Yes No | 2.22 (1.98–2.48)*** | |
| No Yes | 50.6 (41.6–61.6)*** | | No Yes | 7.86 (6.68–9.26)*** | | No Yes | 4.46 (3.84–5.19)*** | |

¹ Multivariate model adjusted for age, sex, geographic region, occupation, monthly income, and comorbidities (including diabetes, hypertension, coronary heart disease, atrial fibrillation, heart failure, chronic kidney disease, and hyperlipidemia).

CONCLUSIONS

Our data indicate that UC (either UT-UC or B-UC) is an independent risk factor for ESRD, especially for women. Our results call attention to the immediate health effects of UC on patients.

