ORIGINAL ARTICLE

Increased risk of urothelial cancer in young and middle aged patients with end-stage renal disease

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Background/Purpose: End-stage renal disease (ESRD) may increase the likelihood of malignancy. The aim of this study is to evaluate the characteristics of increased urothelial cancer (UC) risk in patients with ESRD in Taiwan by a population-based study.
Methods: The standardized incidence ratios (SIRs) for UC among a registered cohort of ESRD in Taiwan during 1997—2002 were calculated using reimbursement data obtained from the Bureau of National Health Insurance (NHI), with the incidence rates of UC in the general population as the reference.
Results: During the study period we identified 58,739 patients with ESRD, 20,939 patients with UC, and 1305 patients with ERSD and UC. Among the 1305 patients with both diseases, 687 developed UC after ESRD had been diagnosed. Using the general population as the reference group, SIRs were 12.9 [95% confidence interval (CI): 12.0—13.9) for all UC cases, 13.9 (95% CI: 12.4—15.0) for bladder cancer, 11.9 (95% CI: 8.6—16.0) for renal cell carcinoma, and 11.6 (95% CI: 10.1—13.1) for upper tract urothelial cancer.
Conclusion: Patients with ESRD are at increased risk for UC in Taiwan, especially women age 50 years and younger. Early and lifelong surveillance of UC is recommended after diagnosis of ESRD.
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Introduction

Various studies carried out in different regions around the world have found that the incidence of malignancy is generally higher in patients suffering from end-stage renal disease (ESRD),[1–4] and renal cell carcinoma (RCC) is especially high in renal cancer after exclusion of cases related to analgesic nephropathy.[2] In Taiwan, several studies have revealed that the incidence rate for urothelial cancer (UC), especially transitional cell carcinoma (TCC), among patients undergoing renal replacement therapy ranges from 0.89% to 1.69%, but RCC is even lower.[5–8]

In our previous study the accumulated incidence rate for UC in the general population using a 200,000 randomized person dataset from the National Health Insurance (NHI) was approximately 0.12%, whereas in patients with ESRD it was much higher (2.1%). Because patients with either major cancer or ESRD in Taiwan can be registered in the "Catastrophic Illness" category, making them exempt from copayments, there is a strong financial incentive for the comprehensive inclusion of such cases. The registry generally requires valid documentation to prevent any potential abuse, thereby preserving the financial system of the NHI. Thus, with this valuable reimbursement database we can initiate a nationwide study to determine whether there is any discernible increase in UC, especially those in the upper tract, in patients with ESRD. The aim of this study is to evaluate the characteristics of UC incidence in this specific population and to select the patients who are at higher risk.

Methods

The NHI scheme was established in Taiwan in March 1995. The National Health Research Institute (NHRI) transforms NHI reimbursement data into files for research. These files have proved invaluable in providing detailed information on the healthcare services used by each patient, including outpatient visits, hospitalizations, and prescriptions. Data collection began in 1996 and by January 1997, the database had already become extremely comprehensive. The records show that the system covered approximately 96% of the total population in Taiwan during 1997–2002.[9] For each outpatient visit, the data contain up to three diagnoses (coded under the International Classification of Diseases, ICD-9), comprising all prescription drugs and dosages (both conventional medicines and Chinese herbal products), any special treatment obtained (including dialysis and kidney transplantation), and the dates of such orders. For hospitalization, up to five diagnoses are recorded. To protect the privacy of all persons registered in the scheme, the identification numbers of all persons contained within the NHI database are encrypted and converted into research files by the NHRI.

Study population

The files in the "Registry of Catastrophic Illness" were obtained for the years 1997–2002; these files include basic records on all patients with catastrophic illnesses, including ESRD, kidney transplants, and UC. A histopathology report is required as a validation document.

Files on patients with diagnoses of ESRD and UC made during the period 1997–2002 were obtained from the registry. UC was identified as bladder cancer (ICD-9 code 188), upper tract urothelial cancer (UT-UC; ICD-9 codes 189.1 and 189.2), and RCC (ICD-9 code 189.0). Cases with ICD-9 code 189.9 were excluded because they did not contain detailed pathological data. Data on patient demographics (sex, date of birth), diagnoses and treatment (the date treatment began and the date of death or transplantation), and duration of renal replacement therapy prior to diagnosis of UC were obtained from the databases and used to calculate the incidence rates of the different types of urinary cancer.

The reference group included all people enrolled in the NHI, or the general population of Taiwan. Thus, patients with UC categorized as ICD-9 codes 188, 189.0, 189.1, and 189.2 were taken as the numerators for the reference population or ESRD patient cohorts. The entire procedure for the selection of the patients is illustrated in the flowchart in Fig. 1.

This study was approved by the Ethics Review Board of the National Taiwan University Hospital, Taipei, Taiwan. In addition, the study complied with personal data protection regulations.

Statistical analysis

The total number of new cases and the incidence rates of UC among patients with ESRD and the reference (general) population were calculated as the number of new patients with UC per 100,000 person-years at risk. The age-stratified incidence rates for UC in the reference population were used to calculate the number of expected cases under the assumption that the reference population had the same cancer experience as patients with ESRD for each age strata. The total number of observed UC cases summed up across all age strata divided by the total number of expected cases was then defined as the standardized incidence ratio (SIR). We then calculated the 95% confidence intervals (95% CIs) under the assumption of Poisson distribution. Potential risk factors, including age and sex, were assessed for any independent association with new occurrences of UTC, concluding with the calculation of age- and sex-stratified incidence rates. All of the above analyses were carried out using the SAS software package, version 8.2 (SAS Institute Inc. Cary, NC, USA).

Results

There were approximately 22 million people registered with the NHI system between the years 1997 and 2002 (as summarized in Fig. 1). Patients with missing information were excluded. During the 6-year cross-sectional study (1997–2002) of the 22 million individuals in the reference group without ESRD, 20,171 developed UC. Among them, 6,816 (34%) were women and 13,355 (66%) were men. The mean age was 65.6 ± 13.9 years. In the reference population, 7% had renal cancer, 34% had renal pelvic and ureteral cancers, and 59% had bladder cancer. Among patients with ESRD, 6% had renal cancer, 30% had renal pelvic and ureteral cancers, and 64% had bladder cancer.