



## Original article

# Risk of stroke in first-ever acute urinary retention: A 10-year population-based study



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## ARTICLE INFO

## Article history:

Received 1 May 2014

Received in revised form

5 January 2016

Accepted 13 January 2016

Available online 21 June 2016

## Keywords:

acute urinary retention

dysautonomia

hypertension

stroke

## ABSTRACT

**Objective:** To examine the 10-year risk of stroke among patients with acute urinary retention (AUR) in Taiwan, using a population-based dataset.

**Methods:** This retrospective cohort study included 38,433 patients aged > 50 years with AUR, with or without catheterization, and 38,433 matched patients without AUR (controls) sourced from the Longitudinal Health Insurance Database from 2001 to 2010. Cox proportional hazards regression was used to evaluate the association between AUR and the risk of stroke during the subsequent 10-year follow-up period, after adjusting for sociodemographic characteristics, hypertension, diabetes, hyperlipidemia, coronary heart disease, and urinary tract infection.

**Results:** Of the 38,433 patients with AUR, 2805 (7.3%) had strokes during the follow-up period compared with 1077 (2.8%) controls (crude hazard ratio, 2.69; 95% confidence interval, 2.5–2.88). After adjusting for potential confounders, risk of stroke was increased in patients with AUR (hazard ratio, 2.36; 95% confidence interval, 2.19–2.53). There was a significant difference in the 10-year stroke-free survival rate between the patients with and without AUR ( $p < 0.001$ , log-rank test). In total, 26.77% of the patients with AUR who experienced a stroke during the 10-year follow-up period had ischemic stroke, while others had hemorrhagic stroke.

**Conclusion:** There was significant difference in the risk of stroke between patients with and without AUR. Preventive measures should be taken for patients with AUR, which may be associated with an increased risk of subsequent stroke. Large-scale population-based studies in other countries and regions are recommended.

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## 1. Introduction

Acute urinary retention (AUR) is a severe problem characterized by a sudden inability to pass urine and is associated with lower abdominal pain.<sup>1</sup> It is found among all age groups<sup>2</sup> and is a major public health issue.

In a worldwide survey on men with benign prostatic hyperplasia,<sup>3</sup> AUR was subcategorized as spontaneous and precipitated. Spontaneous AUR was defined as AUR associated with aging, severe

lower urinary tract symptoms, low peak flow rate, and high post-void residual urine.<sup>4,5</sup> Precipitated AUR was defined as retention associated with a surgical procedure with general, local, or regional anesthesia, bladder over-distension, urinary tract infection, or medication with anticholinergics or sympathomimetic effects.<sup>6</sup>

These two types of AUR are different in prognosis. Precipitated AUR is associated with a much higher 1-year mortality rate (24-fold increase compared with the general population) than spontaneous AUR (10-fold increase).<sup>7</sup> Patients with precipitated AUR often have a higher prevalence of severe underlying comorbid conditions. The reason for the increased mortality rates in both types of AUR is not well understood, although it may be associated with pathophysiological changes that result in or result from AUR.

Acute bladder distension in AUR has been observed to evoke hypertension in clinical patients.<sup>8</sup> Hypertension is associated with

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stroke, and its control has been shown to decrease the long-term rates of incident and recurrent hemorrhagic and ischemic stroke.<sup>9</sup> Sympathetic activity increase is often associated with AUR,<sup>10</sup> and presents as hypertension, tachycardia, and anxiety. In extreme cases of sympathetic activation such as in autonomic dysreflexia in patients with incomplete spinal cord injury, stroke has been reported when AUR triggers autonomic dysreflexia.<sup>11</sup>

Using a population-based database, the present study aimed to examine the 10-year risk of stroke among patients with or without AUR. To the best of our knowledge, the present study is the first to estimate the risk of stroke among patients with previous episodes of AUR.

## 2. Materials and methods

### 2.1. Database

The present study used data sourced from the Longitudinal Health Insurance Database (LHID) 2010. The LHID 2010 contains original medical claims data and registry files for 1 million individuals randomly sampled from all enrollees in the Taiwan National Health Insurance (NHI) program in 2010 ( $n = 23.16$  million). This database is compiled by the Taiwan National Health Research Institute, which also validated that there is no significant difference in sex distribution between the patients in the LHID 2010 and all enrollees under the NHI program. The LHID 2010 is provided to scientists in Taiwan for research purposes, and many researchers have used this dataset for their studies. The present study was exempt from full review by the Institutional Review Board because the LHID 2010 consists of deidentified secondary data released to the public for research purposes.

### 2.2. Study population

We selected all patients who visited ambulatory care centers or were admitted to hospital with a principal diagnosis of AUR (The International Classification of Diseases, 9th Revision, Clinical Modification, ICD-9-CM, code 788.2, retention of urine) or received catheterization (transurethral or suprapubic) procedures from the LHID 2010 from 1 January 1997 to 31 December 2010 ( $n = 167,871$ ).

We excluded patients who had been diagnosed with AUR or undergone urine catheterization during ambulatory care visits or hospitalizations before 2001, with the aim of only including new-onset cases ( $n = 112,423$ ). We also excluded those aged < 50 years to focus more on the group at risk of stroke ( $n = 70,057$ ). Finally, we excluded patients who had been diagnosed with any type of stroke (ICD-9-CM codes 430–438) before 2001 ( $n = 3933$ ). However, as the Taiwan NHI program was initiated in 1995, we could only trace the use of medical services from 1996 to 2010. Therefore, we could not rule out the possibility that some patients had been diagnosed with stroke or AUR before 1996. In total, 38,433 patients with AUR were included as the case group.

The comparison cohort included individuals in the registry of beneficiaries of the LHID 2010 that were matched to the study cohort ( $n = 832,129$ ). We first excluded patients who withdrew before 2010 ( $n = 32,325$ ). We randomly extracted 38,433 individuals (1 for every patient with AUR) matched in terms of age difference < 1 year and the year of index date. We defined the first ambulatory care visit for urine catheterization as the index date for the patients who had ambulatory visits. For patients who were admitted, the date of urine catheterization was defined as the index date. We also checked that no selected individual had ever received a diagnosis of AUR prior to their index ambulatory care visit. Furthermore, we also ensured that none of the selected comparison individuals had ever been diagnosed with AUR since 1996.

The patients were individually tracked until December 31, 2010 to identify those who had had strokes (ICD-9-CM codes 434.91 or 431), starting from their index date.

### 2.3. Statistical analysis

Pearson's Chi-square test was used to examine differences between patients with or without AUR diagnosis, in terms of socio-demographic characteristics (age; monthly income; and the geographical location of the patient's residence: northern, central, eastern, or southern Taiwan) and select comorbid medical disorders that are considered risk factors for stroke and AUR. These comorbid disorders included hypertension (ICD-9-CM codes 401–405), diabetes (ICD-9-CM code 250), hyperlipidemia (ICD-9-CM codes 272.0–272.4), coronary heart disease (ICD-9-CM codes 410–414), and urinary tract infection (ICD-9-CM code 599 or V13.02). These conditions were counted only when they occurred before the date of the stroke, and the interval between the first and last claims was > 1 year. In addition, they were only counted if they occurred either during hospitalization or during ambulatory care visits, and with claim codes for at least 1 year. We also computed the 10-year stroke-free survival rate using the Product-Limit Survival Estimates (SAS, PROC LIFETIME, equivalent to Kaplan–Meier method), and used the log-rank test to compare differences in the risk of stroke for patients with or without AUR. In addition, we used Cox proportional hazards regression to evaluate the association between AUR and the risk of stroke during the study period, after adjusting for sociodemographic characteristics and select comorbid medical disorders. A  $p$ -value < 0.05 (2-sided) was considered to be statistically significant. SAS statistical package (SAS System for Windows, Version 9.2; SAS Institute Inc., Cary, NC, USA) was used to perform all statistical analyses.

### 2.4. Ethics

Our study was approved by the Chang Gung Memorial Hospital Institutional Review Board, and the original LHID 2010 was deidentified by the National Health Research Institute in Taiwan.

## 3. Results

Table 1 shows the distribution of demographic characteristics and comorbid medical disorders for the sampled patients, stratified by whether or not they had AUR. There were significant differences in the distribution of comorbidities, including hypertension (61.21% vs. 50.72%;  $p < 0.0001$ ), diabetes (29.79% vs. 20.61%;  $p < 0.0001$ ), hyperlipidemia (16.9% vs. 15.08%;  $p < 0.0001$ ), coronary heart disease (8.8% vs. 5.08%;  $p < 0.0001$ ), and urinary tract infection (26.48% vs. 12.04%;  $p < 0.0001$ ) between patients with and without AUR. There were no significant differences in the mean age (66.87 years vs. 66.94 years;  $p = 0.411$ ), monthly income, and urban or rural residency of the patients.

Table 2 shows the percentage of stroke during the 10-year follow-up period among patients with and without AUR. In the total sample of 76,866 patients with or without AUR, 3882 (5.05%) patients had strokes during the 10-year follow-up period. These included 2805 patients with AUR (7.3% of all patients who had AUR) and 1077 patients who did not have AUR (2.8% of all patients who did not have AUR). There was a significant difference in the 10-year stroke-free survival rate between the patients with and without AUR ( $p < 0.001$ , log-rank test). The results of product-limit survival estimates (survival analysis) are shown in Figure 1.

Table 2 also presents the crude and adjusted hazard ratios (HR) for stroke comparing patients with or without AUR. After censoring cases who died from nonstroke related causes during the 10-year

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