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ORIGINAL ARTICLE

Prostate Disease

# Transurethral resection of prostate for acute urinary retention is linked to shorter survival in younger men

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**It is largely unknown whether lower urinary tract symptoms (LUTS) or acute retention of urine (AROU) is linked to shorter life expectancy in men. We conducted a multicenter, retrospective database analysis of patients undergoing transurethral resection of prostate (TURP) to study their relationships. Multivariate Cox regression analysis and Kaplan–Meier analysis with stratification to age and indication of TURP were performed. We further performed an age- and sex-matched survival analysis with the general population using data from the Census and Statistics Department of the Hong Kong Special Administrative Region (Hong Kong, China). From January 2002 to December 2012, 3496 patients undergoing TURP were included in our study, with 1764 patients in the LUTS group and 1732 patients in the AROU group. Old age, ischemic heart disease, cerebrovascular accident, and AROU were risk factors of mortality. Patients aged <70 years (adjusted hazard ratio [HR]: 1.52, 95% confidence interval [CI]: 1.11–2.09, *P* = 0.010) and 70–80 years (adjusted HR: 1.39, 95% CI: 1.15–1.70, *P* = 0.001) in the AROU group had worse survival than those in the LUTS group, but such difference was not demonstrated in patients aged >80 years. Compared to the general population, younger patients in the LUTS group appeared to have better survival (<70 years, *P* = 0.091; 70–80 years, *P* = 0.011), but younger patients in the AROU group had worse survival (<70 years, *P* = 0.021; 70–80 years, *P* = 0.003). For patients aged >80 years, survival was similar with the general population in both the LUTS and AROU groups. In conclusion, AROU at young age was associated with mortality, while early detection and management of LUTS may improve survival.**

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## INTRODUCTION

Benign prostatic hyperplasia (BPH) is a common condition causing lower urinary tract symptoms (LUTS). However, there are many causes of LUTS other than BPH, including detrusor underactivity and nocturnal polyuria.[1] The occurrence of LUTS represents not only the possibility of BPH but also a reflection of patients' underlying medical conditions.[2,3] In a recent meta-analysis,[4] moderate-to-severe LUTS was associated with increased incidence of major adverse cardiac events, including angina pectoris, acute myocardial infarction, chronic ischemic heart disease, and transient ischemic attack of cerebrovascular accident. These major adverse cardiac events can be life-threatening and may have deleterious effects on patients' survival.

Patients with BPH may present with acute retention of urine (AROU). Presumably, AROU reflects a more severe degree of symptomatology than LUTS. In the general population, the reported incidence of AROU ranged from 2.2 to 6.8 per 1000 men per year.[5,6] Unfortunately, many patients may overlook their existing LUTS until they developed AROU, such that appropriate medical advice may not be sought earlier on. In a retrospective cohort study involving 56 958 men, AROU was the first presenting symptom of BPH in 49% of all AROU cases.[6] We hypothesize that men with AROU are more likely to have acquired underlying medical problems that are progressive, irreversible, and more severe, whereas men with mere LUTS still possess relatively better general health condition and hence longer life expectancy. Following that, early detection and treatment of LUTS may put forward the recognition of any underlying medical conditions and may have an impact on patients' survival. In this study, we investigated the association of mortality with LUTS and AROU, respectively, in patients undergoing transurethral resection of prostate (TURP), and further compared their survival probabilities, respectively, with the general population.

## PATIENTS AND METHODS

This study was conducted in accordance with the Declaration of Helsinki. The study protocol was approved by the Clinical Research Ethics Committee of the New Territories East Cluster, Hong Kong, China. As this is a retrospective review, informed consent from the patients is not required by the committee of the institute review board.

### *Study design*

We performed a retrospective analysis of all patients undergoing TURP at three local hospitals (Prince of Wales Hospital, Alice Ho Miu Ling Nethersole Hospital, and North District Hospital) in Hong Kong (China) from January 2002 to December 2012. We utilized a territory-

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wide electronic patient record system (the Clinical Management System, Hospital Authority, Hong Kong, China), which is a standardized, computerized system that records all diagnostic and procedural codes of patients based on the 9th edition of the International Classification of Diseases for data retrieval. The patient list was retrieved using procedural code of 60.2 (transurethral prostatectomy). In Hong Kong (China), it is mandatory for the operating urologist to input a coded diagnosis, *i.e.*, the indication of TURP, into the operation record. The diagnostic codes entered during TURP were used to stratify patients into the LUTS group and the AROU group. Patients with diagnostic codes including 600.00 (hypertrophy of prostate without urinary obstruction), 600.20 (benign localized hyperplasia of prostate without urinary obstruction), 600.90 (hyperplasia of prostate, unspecified, without urinary obstruction), 788.4 (frequency of urination and polyuria), 788.61 (splitting of urinary stream), 788.62 (slowing of urinary stream), 788.63 (urgency of urination), 788.64 (urinary hesitancy), 788.65 (straining on urination), 788.69 (other abnormality of urination), and 788.9 (lower urinary tract symptoms) were categorized into the LUTS group. Patients with diagnostic codes including 600.01 (hypertrophy of prostate with urinary obstruction), 600.21 (benign localized hyperplasia of prostate with urinary obstruction), 600.91 (hyperplasia of prostate, unspecified, with urinary obstruction), and 788.2 (retention of urine) were categorized into the AROU group. Patients who had diagnostic codes of 185 (malignant neoplasm of prostate), 598 (urethral stricture), 596.0 (bladder neck obstruction), and 596.54 (neurogenic bladder) were excluded. Patients' background medical conditions were also retrieved. Diagnostic codes including 490 (bronchitis, not specified as acute or chronic), 491 (chronic bronchitis), 492 (emphysema), and 496 (chronic airway obstruction, not elsewhere classified) were grouped under term "chronic obstructive pulmonary disease." Diagnostic codes including 410 (acute myocardial infarction), 411 (other acute and subacute forms of ischemic heart disease), 412 (old myocardial infarction), and 414 (other forms of chronic ischemic heart disease) were grouped under the term "ischemic heart disease." Diagnostic codes including 431 (intracerebral hemorrhage), 434 (occlusion of cerebral arteries), and 436 (acute, but ill-defined, cerebrovascular disease) were grouped under the term "cerebrovascular accident."

### *Statistical analyses*

For the comparison of the baseline characteristics between the two groups, independent samples *t*-test and Mann-Whitney U test were used for continuous variables, as appropriate, and Chi-square test was used for categorical variables. Univariate and multivariate Cox regression analyses were performed to investigate for predictors of mortality. Kaplan–Meier analysis was performed to compare between the LUTS and the AROU groups, with stratification according to age groups of <70 years, 70-80 years, and >80 years.

We further compared the survival probabilities of both the LUTS group and the AROU group with those from the general population, using the method by Ederer.[7,8] Study patients in our cohort were matched to the general population by age and sex in a 1:1 ratio. Survival probabilities of the general population were derived from the life tables from the Census and Statistics Department of the Government of the Hong Kong Special Administrative Region (Hong Kong, China).[9] The expected survival probabilities were calculated based on a 1-year calendar interval. For example, in order to match a 60-year-old man who had TURP done in 2008, the expected death rate in the first year would be the rate for people in the general population who were 60 years old in 2008, and the expected death rate in the second year would be the rate for people in the general population who were 61 years old in 2009, and this process was continued annually. Kaplan–Meier analysis was performed with the significance level being determined by log-rank test. $P < 0.05$ was considered statistically significant. All statistical analyses were performed using SPSS version 20.0 (IBM Corp., Armonk, NY, USA) or R package (R Foundation for Statistical Computing, Vienna, Austria; https://www.R-project.org).

## RESULTS

### *Baseline characteristics*

From January 2002 to December 2012, 3664 patients underwent TURP at the three hospitals. One hundred and sixty-eight patients were excluded because of diagnoses of urethral stricture, bladder neck stenosis, prostate cancer, and neurogenic bladder, resulting in 3496 patients in the final analyses with a median follow-up of 5.4 years. Among them, 1764 patients underwent TURP for LUTS and 1732 patients underwent TURP for AROU. The AROU group had an older age than the LUTS group (mean ± standard deviation [s.d.]: 74.0 ± 8.3 years *vs* 70.7 ± 8.2 years, $P < 0.001$). For the preexisting medical conditions, the AROU group had higher rates of chronic obstructive pulmonary disease (18.0% *vs* 13.7%, $P < 0.001$), ischemic heart disease (23.3% *vs* 18.3%, $P < 0.001$), and cerebrovascular accident (6.4% *vs* 4.7%, $P = 0.033$) than the LUTS group (**Table 1**).

### *Predictors of overall survival*

Old age, ischemic heart disease, cerebrovascular accident, and TURP for AROU were associated with worse survival upon both univariate and multivariate Cox regression analyses (**Table 2**). Among them, age of >80 years had the highest hazard ratio (HR) of 5.31 (95% CI: 4.35–6.46, $P < 0.001$) upon multivariate analysis. Chronic obstructive pulmonary disease was associated with worse survival upon univariate analysis, but became insignificant upon multivariate analysis.

### *Survival analysis among LUTS group, AROU group, and the general population of the same age structure*

We compared the survival between the LUTS and the AROU groups, according to the age groups of <70 years, 70–80 years, and >80 years, respectively (**Figure 1**). The AROU group had significantly worse survival than the LUTS group in patients aged <70 years (HR: 1.52, 95% CI: 1.11–2.09, $P = 0.010$), and in patients aged 70–80 years (adjusted HR: 1.39, 95% CI: 1.15–1.70, $P = 0.001$), after adjustment for chronic obstructive pulmonary disease, ischemic heart disease and cerebrovascular accident. Whereas, there was no difference in survival between the LUTS and AROU groups in the age group of >80 years (adjusted HR: 0.96, 95% CI: 0.76–1.21, $P = 0.720$). When comparing to the expected survival of the respective age groups of men in the general population, based on the mortality rate of each respective age shown in the life tables across the whole study period, there is a trend that patients aged <70 years in the LUTS group had better survival than the general population ($P = 0.091$). For patients aged 70–80 years, the LUTS group had significantly better survival than the general population ($P = 0.011$). However, no survival difference between the LUTS group and the general population ($P = 0.820$) was observed for patients aged >80 years (**Figure 2**).

In contrast, patients aged <70 years ($P = 0.021$) and 70–80 years ($P = 0.003$) in the AROU group had worse survival than the general population, respectively. Whereas, for patients aged >80 years, there was no survival difference between the AROU group and the general population ($P = 0.820$) (**Figure 3**).

## DISCUSSION

Traditionally, male LUTS has been thought to be largely related to bladder outlet obstruction secondary to BPH. However, the occurrence

**Table 1: Baseline characteristics in the cohort**

| *Variables* | *LUTS group (n=1764)* | *AROU group (n=1732)* | *P* |
|---|---|---|---|
| Age (year), mean ± s.d. | 70.7 ± 8.2 | 74.0 ± 8.3 | <0.001 |
| Age group (year), *n* (%) | | | |
| <70 | 810 (45.9) | 540 (31.2) | <0.001 |
| 70–80 | 727 (41.2) | 764 (44.1) | |
| >80 | 227 (12.9) | 428 (24.7) | |
| Chronic obstructive pulmonary disease, *n* (%) | 242 (13.7) | 312 (18.0) | <0.001 |
| Ischemia heart disease, *n* (%) | 323 (18.3) | 404 (23.3) | <0.001 |
| Cerebrovascular accident, *n* (%) | 83 (4.7) | 111 (6.4) | 0.033 |

LUTS: lower urinary traction symptoms; AROU: acute retention of urine; s.d.: standard deviation

**Table 2: Univariate and multivariate cox regression analyses on overall survival**

| *Co-variates* | *Unadjusted HR (95% CI)* | *P* | *Adjusted HR (95% CI)* | *P* |
|---|---|---|---|---|
| Age (year) | | | | |
| <70 | Reference | | Reference | |
| 70–80 | 2.92 (2.43–3.51) | <0.001 | 2.64 (2.19–3.17) | <0.001 |
| >80 | 7.03 (5.80–8.51) | <0.001 | 5.31 (4.35–6.46) | <0.001 |
| Chronic obstructive pulmonary disease (present) | 2.70 (2.35–3.11) | <0.001 | 1.12 (0.83–1.51) | 0.448 |
| Ischemia heart disease (present) | 3.09 (2.71–3.53) | <0.001 | 1.95 (1.42–2.69) | <0.001 |
| Cerebrovascular accident (present) | 3.19 (2.63–3.87) | <0.001 | 1.47 (1.12–1.94) | 0.005 |
| TURP | | | | |
| For LUTS | Reference | | Reference | |
| For AROU | 1.70 (1.49–1.94) | <0.001 | 1.33 (1.16–1.52) | <0.001 |

LUTS: lower urinary traction symptoms; AROU: acute retention of urine; TURP: transurethral resection of prostate; CI: confidence interval; HR: hazard ratio

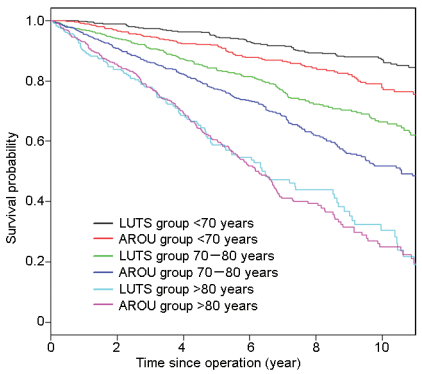


**Figure 1:** Overall survival in the LUTS and AROU groups stratified by age. LUTS: lower urinary traction symptoms; AROU: acute retention of urine.

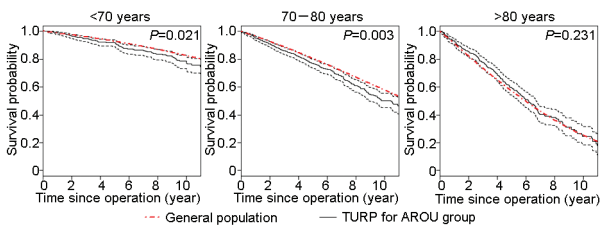


**Figure 3:** Overall survival comparison between the AROU group and the age- and sex-matched general population. The dotted lines show the upper and lower limits of the 95% confidence interval. AROU: acute retention of urine; TURP: transurethral resection of prostate.

of LUTS can be due to other causes such as detrusor underactivity and nocturnal polyuria. Preexisting medical conditions may play an important role in patients presenting with LUTS. The association between LUTS and cardiovascular events has been demonstrated

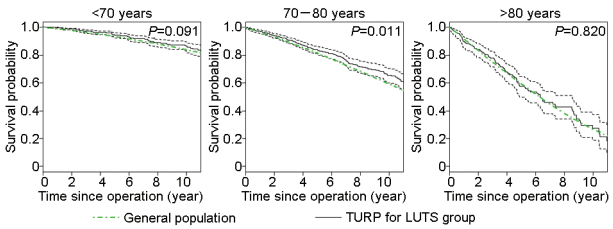


**Figure 2:** Overall survival comparison between the LUTS group and the age- and sex-matched general population. The dotted lines show the upper and lower limits of the 95% confidence interval. LUTS: lower urinary traction symptoms.

previously.[4] It was believed that LUTS and cardiovascular disease might share common pathophysiological mechanisms.[10,11] As urinary retention could represent a more severe form of symptomatology, we hypothesize that the occurrence of LUTS may serve as an early indicator of any underlying medical conditions.

Previous studies have investigated the association between prostatic surgery and mortality. In the study by Roos *et al*.,[12] it was surprising to find that patients undergoing TURP had higher long-term mortality when compared to open prostatectomy. The authors concluded that their results were likely to be explained by confounding factors, as they expected patients undergoing open prostatectomy would have fewer comorbidities than those undergoing TURP. In another study by Concato *et al*.,[13] it was shown that patients undergoing TURP were in general older patients with more comorbidities, and long-term mortality did not differ after adjusting for confounding factors. A subsequent large-scale nation-wide study of 23 123 cases did not demonstrate any excess risk of myocardial infarction or mortality after TURP when compared to open prostatectomy.[14] However, all three studies did not provide any information on the indication of surgery, and further analysis comparing the mortality between LUTS and AROU could not be performed.

In the study by Armitage *et al*.,[15] a database analysis on men presenting to the hospital with AROU was performed. Patients were defined to have spontaneous AROU if they had acute urinary retention being recorded in the first diagnostic field, or BPH being recorded as the primary diagnosis, and acute urinary retention being recorded in another diagnostic field. In all other cases, patients were defined to have precipitated AROU. The results showed that patients with precipitated AROU had much worse standardized mortality ratios than patients with spontaneous AROU. Mortality increased strongly with age and comorbidity; therefore, the authors concluded that it would be important to have multidisciplinary care to identify and treat comorbid conditions in patients presenting with AROU. However, the study did not include patients presenting with LUTS; therefore, whether early detection of the underlying disease could reduce mortality is unknown.

In this study, we included patients who had TURP performed, and we excluded patients who had urethral stricture, bladder neck stenosis, and prostate cancer. By this, we assume that all patients had histologically confirmed BPH; TURP was able to alleviate bladder outlet obstruction in the vast majority of the cases; and they should not suffer from prostate- or bladder outlet obstruction-related problems after the surgery. We also excluded patients with neurogenic bladder, as underlying conditions including spinal cord injury, multiple sclerosis, or spina bifida are well-known causes of urinary retention, but vary widely from the general population with BPH. Concerning the preexisting medical conditions, we would like to point out that the diagnoses of chronic obstructive pulmonary disease, ischemic heart disease, and cerebrovascular accident were stringently coded in the hospitals of our cluster due to the interdepartmental policy; therefore, we expect highly reliable and accurate values for these diagnoses.[16–18] Other medical conditions including diabetes mellitus, hypertension, dyslipidemia, and chronic kidney disease were not routinely screened in our patients and were less likely to be the reason for acute hospital admission; therefore, the data may be inaccurate and we decided not to retrieve data on these conditions.

As the prevalence of BPH increases with age, it is expected that the occurrence of AROU also increases with age. In this study, we noted that the AROU group was associated with worse survival than the LUTS group in both the <70 years' and 70–80 years' age groups. This difference, however, was not detected in patients of the older age group of >80 years. Therefore, we postulate that AROU in a younger patient is probably associated with more significant underlying medical illness other than enlarged prostate alone as compared to the men of the same age in the general population. Both the univariate and multivariate analyses showed that ischemic heart disease and cerebrovascular accident were risk factors of mortality; therefore, we suspect that these conditions may play a more significant role in particular for younger patients presenting with AROU. As such, we believe that the occurrence of AROU may reflect the degree of severity of the preexisting medical conditions which may be more clinically significant in younger patients presenting with AROU. The analyses, however, were limited by the imbalance in the baseline characteristics between the LUTS and AROU groups. Therefore, we further compared the survival probabilities of the LUTS and AROU groups with the general population by matching every study patient in the LUTS and AROU groups with the general population. The expected survival probabilities in the general population were derived from the Hong Kong (China) life tables.[9] This is a common, well-accepted methodology being used in the literature.[7,8]

The fact that AROU patients of age <80 years had shorter than expected survival further supports our postulation that AROU is a sign prognosticating significant underlying medical illness. As to the observation that LUTS group patients outlive those men of the same age structure in the general population, we postulate that the patients in the LUTS group were more self-cautious and sought medical advice at an earlier stage and, therefore, would have detected any significant medical conditions much earlier on. This resulted in an even better survival than the general condition in younger patients. This observation is not evident in the older age group for which the plausible explanation remains to be elucidated by further study.

Since we only included patients with TURP performed, and excluded those with urethral stricture, bladder neck stenosis, and prostate cancer, we assume that they would not suffer from prostate- or bladder outlet obstruction-related problems after the surgery. However, it is possible that patients might have suffered from deleterious effects accounted by BPH and its related complications, which have already occurred before surgery. It raises the question whether offering TURP at an earlier stage of the BPH, *i.e.*, before the occurrence of AROU, could prevent patients suffering from BPH and its related complications, and therefore improve patients' survival in long run. However, complications related to BPH including hematuria and recurrent urinary tract infection usually resolve upon appropriate treatment without significant long-term sequelae. Urinary retention with obstructive uropathy leading to irreversible renal impairment is possible, but the risk of renal insufficiency in patients with BPH is minimal,[19] and the association between BPH and chronic kidney disease is not well defined.[20] Therefore, we believe that the difference in survival outcomes cannot be explained by earlier TURP alone.

There are several limitations in this study. First, the data were retrieved from a computerized electronic system. The study is retrospective in nature and there is no standardized screening or follow-up protocol; hence, the results may be inaccurate. For this reason, we decided not to include medical conditions such as diabetes mellitus, hypertension, dyslipidemia, and chronic kidney disease. We only included major medical problems, including chronic obstructive pulmonary disease, ischemic heart disease, and cerebrovascular accident, as we expected high positive predictive values of these diagnoses being input. Second, although we included only patients whose bladder outlet obstruction was treated following TURP and excluded those with urethral stricture, bladder neck stenosis, and prostate cancer, one can still argue that there exists the possibility of recurrence of bladder outlet obstruction due to the prostate regeneration with time and such recurrent bladder outlet obstruction may impose unknown confounding effect on the long-term survival. However, such risk of recurrent bladder outlet obstruction is small, and even if it exists, it will similarly affect both the LUTS and AROU groups. Third, selecting only patients with TURP performed may lead to a selection bias, with the general health status of our cohort being better than the general population. This may explain why the LUTS group had better survival than the general population. However, this would not be able to explain why the AROU group had worse survival than the general population. Fourth, although our results do suggest an association between AROU and mortality in younger patients, due to the retrospective nature of the study, we could not further examine the underlying pathophysiological mechanisms. Fifth, we are not able to retrieve information on the prostate size and the weight of prostate tissue being removed upon TURP. Therefore, we could not perform subgroup analyses on the impact of prostate size on mortality in our cohort.

## CONCLUSION

Our results showed that AROU at young age (<80 years old) is associated with higher mortality when compared to the general population. This is potentially preventable as young patients with LUTS

had similar, if not better, survival outcomes as the general population. Early awareness to seek medical advice for LUTS alone together with early management of coexisting medical conditions may lead to better overall survival. The results are hypothesis generating and further studies are needed to confirm such postulation. Prospective cohort studies may help provide more accurate information, but a long-term follow-up is needed to detect any significant difference.

## AUTHOR CONTRIBUTIONS

JYCT developed the study protocol and drafted the manuscript. CKC developed the study protocol, drafted, and revised the final manuscript. PKFC, CHY, and HMW collected the data. MHW and CHL performed the data analyses. ESYC, SSMH, and CFN made critical suggestions to the manuscript. All authors read and approved the final manuscript.

## COMPETING INTERESTS

All authors declared no competing interests.

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