

## THE NATURAL HISTORY OF NOCTURIA 10 YEARS LONG-TERM FOLLOW-UP IN MALE PATIENTS AGED 40 YEARS AND ABOVE

### Hypothesis / aims of study

Nocturia is a condition where the patient has to wake up at night one or more times to void and the condition has recently been recognised as a clinical entity in its own right (ICS 2002). To date there are few published data on the natural history of nocturia. Cross-sectional surveys have indicated that the prevalence and severity of nocturia increase with age - but to our knowledge these findings has never been confirmed in a longitudinal follow-up, and this is the first study to report 10 year minimum follow-up data in nocturia.

As nocturia is considered one of the most troublesome lower urinary tract symptoms (LUTS), knowledge of its natural history is important in order to better advise the patient as to his or her management and the likelihood for progression. The primary objective of this study is to estimate the change in prevalence of nocturia over a 10 year period in hospital-based records, thought to be a representative sample of the adult community. The secondary objective of this study is to examine the prevalence of nocturnal polyuria (defined as mean night-time urine production exceeding 33% of the daily 24h urine production, averaged over a 1-week period at baseline and follow-up). Differences in the relationship between change in prevalence of nocturia and general health status were also investigated.

### Study design, materials and methods

The Urodynamic Unit at our hospital has a comprehensive record system established in 1972. The records stored in the Urodynamic Unit were searched for flow clinic patients who had completed FVCs from 1991-1994, approximately 6,000 in total. 608 men selected aged 40 years or more at the time of completion of the original FVCs were included in the study. The patients in the flow clinic are referred from general practitioners and are considered to be more representative for normal population. Each patient for flow studies completed a 7-day frequency volume chart (FVC). The data from the original, 7day FVC was abstracted and entered on a database designed for this study.

As requested by the local ethics committee, we contacted these patients General Practitioners (GP) to get permission before contacting the patients. We managed to obtain details of most of GPs for approximately 80% of selected sample.

Based on the raw data from the original and new FVCs, the following variables were calculated over 7 days: Mean daily micturition frequency, Mean nocturia frequency, Mean daily fluid intake, Maximum voided volume, Mean voided volume, and Maximum duration between day voids. In order to obtain the necessary data on nocturnal polyuria, additional variables were calculated base on raw data from original FVCs: Mean day-time voided volume, Mean night-time voided volume, and Mean daily 24h urine production. Using a postal survey the patients were asked to complete a new 7-day FVC and the ICIQ Nocturia module.

Paired t test was used to examine the difference between the NF recorded over 10 years ago and now. Linear Regression was carried out to examine the relationship between age and NF, as well as between the degree of NF with QoL. Two scores from ICIQ Nocturia form indicate (i) how much a person was bothered by the NF, (ii) how much NF has an impact on QoL.

### Results

(1) Sample information.

a) Number of subjects

A total of 608 male patients were selected, 528 GPs got our letter asking about the patient's current condition and whether he was suitable for the survey. 448 GP replied, in which 236 patients were indicated suitable for the study; the remaining 212 patients were not, for varied reasons – 112 of them had moved away without new addresses forwarded, 80 had died during the last 10 more years, 19 had some health or mental problems and 1 without any reason given. Therefore, the study documents were sent through the post to the 236 suitable patients. However, 162 of them failed to respond. 74 did reply either by post or telephone. Out of them, we obtained 51 patients' newly filled FVCs and the ICIQ nocturia questionnaire. The other 23 told us that they do not wish to take part in the study.

b) Age

	Mean (N=51)	Range	95% confidence interval f mean
Age at original FVC	61	40-74	59.0 – 63.8
Age now	76	53-88	73.3 – 78.3

The average time length between the original FVC and the new FVC was 14 years.

c) Urinary problem related treatments during more than 10 years time period

Over the 10 or more years, 34 out of 51 patients (67%) had been treated for either prostate or bladder problems. 68% (n=23) and 32% (n=11) of these patients had had surgery and medications respectively.

(2) The change of Nocturia frequency (NF)

NF was relatively unchanged, being 1.86 previously (95%CI: 1.6 – 2.2) and 1.93 (95%CI: 1.6 – 2.2) from the most recent FVC. The proportion of patients having NF less or greater than 2 times per night also did not significantly changed (47% and 53%).

(3) Prevalence of nocturnal polyuria at baseline and follow-up

At baseline, the proportion of people with nocturnal polyuria was 60% (30 out of 50 patients), and had increased to 75% (36 out of 48 patients) over 10 years period. The degree of nocturnal polyuria between then and now showed a

marked significant difference in means 36% and 42% ( $t = -3.2$ ,  $df=46$ ,  $p < 0.005$ , with the 95% interval being 33% - 39% and 38% - 46% respectively).

(4) Impact of nocturia frequency at follow-up on QoL

Linear Regression analysis showed that increasing nocturia episode had a strong positive relationship with an increase in the patients' feeling of bothersome,  $r=0.37$ ,  $F=7.57$ ,  $p < 0.01$ . However, the relationship between NF and overall QoL was not significant,  $r= 0.19$ ,  $F=1.93$ ,  $p > 0.18$ . This suggested that, although they do feel annoyed by NF, it did not significantly impact on their daily life.

(5) How age related to nocturia frequency

Although, at baseline there was only a trend for age and NF to be related ( $r=0.24$ ,  $F=3.01$ ,  $p < 0.09$ ), after more than 10 years time period, the relationship increased and became statistically significant,  $r=0.28$ ,  $F=4.15$ ,  $p < 0.05$ , showing that with increasing age, NF tends to become worse.

Interpretation of results

The study was originally an ambitious one, which planned to survey 1200 men and women to investigate the change in prevalence of nocturia over a 10 year period. The major setback to the plan came from the loss of a large proportion of the original sample. There are multiple factors causing the loss, the major one is that many patients have left the area over the 10 years period. The second reason was the lack of GP information for a significant number of patients and proportion of them did not respond to our letter. Therefore, we lost more than 25% of the original sample (160 out of 608). The third reason causing the sample to diminish substantially was the proportion of patients who chose not to take part in the study. The smaller sample size may have lead to the study results being less representative, but, on the other hand, the sample reported here was also a truly random one which indeed represents a male population who have been troubled by urinary related problems over a period of more than 10 years time.

Concluding message

In older men, NF tended to increase with age, however, as far as individuals are concerned, NF appears not to changed much over a more than 10 years of time period. This may be due to the fact that majority of the subjects had been treated for their urinary related diseases, and some remained on medication. The NF on average remains less than twice per night, which was bothersome, but, in general, did not have a significant impact on overall daily life. On the other hand, it was also found that, over time, the degree of nocturnal polyuria significantly increased.

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**HUMAN SUBJECTS:** This study was approved by the Southmead Research Ethics Committee, Bristol, UK and followed the Declaration of Helsinki Informed consent was obtained from the patients.