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Reference Values for the Nocturnal Bladder Capacity Index

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Aims: The Nocturnal Bladder Capacity Index (NBCi) has been reported to be useful in distinguishing between nocturia caused by low bladder capacity and nocturnal polyuria. This paper aims to calculate reference values for NBCi from an asymptomatic population by comparing these with NBCi values from patients with lower urinary tract symptoms (LUTS) to obtain an indication of the sensitivity with which the NBCi detects low nocturnal bladder capacity. This paper also compares the sensitivity of rounded and unrounded calculations of NBCi. **Methods:** Computer processed 3-day bladder diaries from 253 asymptomatic volunteers and 184 female patients with LUTS were analyzed. NBCi values were calculated from each diary using rounded and unrounded formulae. 90th and 95th centile NBCi cutoff values were obtained from frequency distributions. **Results:** NBCi reference values from the asymptomatic group were 1.1 (unrounded) and 0.7 (rounded) for 90th centile, and 1.3 (unrounded) and 1.0 (rounded) for 95th centile. The use of the rounded formula gave identical NBCi values despite a large variation in V_n/V_{max} ratios whereas unrounded NBCis varied continuously with V_n/V_{max} ratios. The unrounded formula found significantly more elevated NBCis in the patient group. **Conclusion:** We suggest that an unrounded NBCi of 1.3 be considered a cutoff point above which reduced nocturnal bladder capacity should be investigated as a cause of nocturia. Rounding the NBCi lead to an underestimation of elevated values in a population of female patients with LUTS. *Neurourol. Urodynam. 30:52–57, 2011.* © 2010 Wiley-Liss, Inc.

Key words: bladder capacity; bladder diary; diagnosis; frequency–volume chart; nocturia

INTRODUCTION

Nocturia is defined as waking at least once during the night to urinate. It is caused by reduced bladder capacity, nocturnal polyuria, or a combination of the two.

The relative contributions of bladder capacity and night time urine production are determined by analysis of the voiding diary. The Nocturnal Bladder Capacity Index (NBCi), derived from the voiding diary, is a quantitative method of comparing nocturnal bladder capacity with 24-hr bladder capacity (maximum voided volume, V_{max}),[1,8] and has been shown to be empirically useful in comparing multifactorial etiologies of nocturia.[2–7] The aim of this study is to improve NBCi as a clinical measurement of nocturnal bladder capacity by defining asymptomatic reference values for it.

The NBCi is based on the difference between the "predicted" and actual number of night voids. The more the actual number of night voids exceeds the predicted night voids, the lower is night bladder capacity.

Assuming the following abbreviations for the variables:

F_{n-p} "predicted" number of night voids
F_n actual number of night voids
V_n nocturnal voided volume
V_{max} maximum volume per void.

The current formulae for calculating NBCi are[8]:

$$F_{n-p} = \text{Round-up}[(V_n/V_{max})-1]$$
$$\text{NBCi} = F_n - F_{n-p}$$

The prediction of the number of night voids assumes that night urine production is eliminated by voids at bladder capacity (as defined by V_{max}). Thus, F_{n-p} is calculated by dividing night volume by V_{max}, subtracting 1, and rounding up to the next largest number. One is subtracted from V_n/V_{max} because the last void of the urine produced at night occurs after waking in the morning and is thus classified as a day time void. The predicted number of nightly voids is rounded up based on the assumption that people will void soon after awakening in the morning irrespective of whether the volume in their bladder is near or far from their bladder capacity.

The primary goal of this paper is to obtain reference values of NBCi from an asymptomatic population. There are reports of NBCi values in symptomatic populations,[1,2,4,6–8] but we have found no published NBCi reference values from asymptomatic populations. To develop NBCi reference values, we obtain a frequency distribution of NBCi from asymptomatic volunteers and test for possible influences of age, sex, and 24-hr urine volume (V24).

A secondary goal of this paper is to compare NBCi values in women with lower urinary tract symptoms (LUTS) with the asymptomatic reference values to obtain an indication of the sensitivity with which the NBCi detects low nocturnal bladder capacity. (For example, NBCi detection of low nocturnal bladder capacity in only 1% of patients with LUTS would be evidence that the NBCi is too insensitive to be clinically useful.)

In the course of our data analysis, we discovered some unexpected effects of rounding up F_{n-p} that led us to adopt as a tertiary goal a comparison of the sensitivity of an "unrounded" calculation of NBCi with the rounded NBCi.

Chris Winters led the review process.
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MATERIALS AND METHODS

Test Subjects

Male and female volunteers were recruited by advertisement at 4 centers,[9,10] and women complaining of LUTS were recruited from 2 centers.[11] Selection of the asymptomatic subjects was based on a questionnaire designed to rule out LUTS and disorders, medications, and surgeries that might affect urination—for example, diabetes, heart disease, neurologic disorders, and previous incontinence surgery.[1] Those with nonstandard sleep patterns (e.g., night shifts) were also excluded. Additional information on the asymptomatic population can be found in Amundsen et al.[9] At each center, the study was carried out under either IRB or Ethics Committee approval.

Voiding Diary Collection and Analysis

Identical 3-day voiding diaries were collected from patients and asymptomatic volunteers. The diary forms were designed to optimize computer handwriting recognition. Data from the handwritten diaries were entered into a computer via intelligent character recognition software (Life-Tech, Stafford, TX) to allow analysis. To conform to ICS definitions, "start of day" was defined as "time you leave your bed for the day" and "bed time" as "time you turn the lights out in preparation for sleep."

For each diary, V24, production rate, and frequency were calculated together with minimum, maximum, and average voided volumes. A "urinated but volume not recorded" checkbox accommodated voids where subjects were unable to measure volume (e.g., if the subject was in a restaurant). The computer filled in these missing volumes with the median of all recorded voided volumes. (All diaries where volumes of fewer than 25% of all voids or 10% of all night voids were recorded were excluded. Diaries excluded for this reason comprised about 1% of all collected diaries.)

Rounded and unrounded NBCis were calculated as follows:

$$\text{Rounded NBCi} = F_n - \text{Round-up}[(V_n/V_{max}) - 1]$$

$$\text{Unrounded NBCi} = Fn - (V_n/V_{max} - 1)$$

Statistical Analysis

The difference between the mean NBCis of males and females was assessed with the *t*-test. As we used frequency distributions to determine cutoff limits, we used chi-squared tests to test for differences between frequency distributions. Our descriptive statistics include distribution skewness, which was calculated as described by Neter et al.[12] Chi-squared tests were used to assess the differences in instances of low NBCis. Regression analysis was performed to investigate the effect of age, V24, and F_n on NBCi. Our criterion for significance was a *P*-value <0.05.

RESULTS

Test Subjects

Voiding diaries were collected from 161 asymptomatic females (age range: 20–82),[9] 92 asymptomatic males (age range 21–85),[10] and 184 female patients complaining of LUTS (age range 18–83).[11] One hundred sixty-three of the patients had urodynamics that included pressure flow studies and subtracted cystometry. Table I lists the symptoms and signs within the patient population, and Figure 1 shows the frequency distribution of F_n in the patient population. The distribution is highly skewed to the right. 24.3% of the patients had nocturia >2.

TABLE I. Symptoms Within the Patient Group

Symptom/sign	Number	%
Urgency	105	57.1
Prolapse	64	34.8
Mixed incontinence	54	29.3
Stress incontinence	35	19.0
Urge incontinence	22	12.0
Bladder pain	11	6.0
None of above	34	18.5
Indeterminate[a]	30	16.3

[a]Patients with LUTS whose medical records were inadequate to further characterize the LUTS.

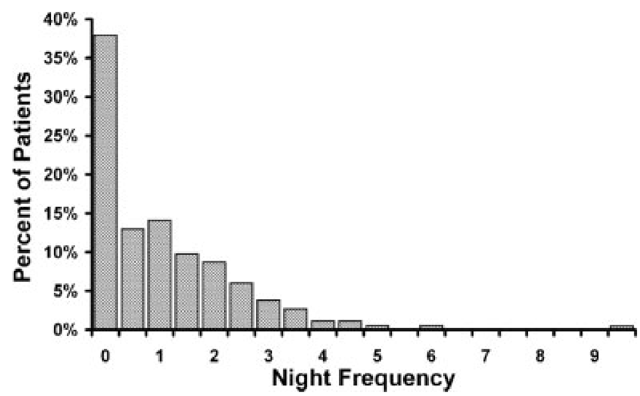

Fig. 1. Distribution of night frequencies among patients with LUTS.

Descriptive Statistics

Table II summarizes descriptive statistics of the NBCi from the asymptomatic and patient populations. Positive skewness measurements indicate that all frequency distributions are skewed to the right. The patient distributions tend to be more highly skewed than the analogous asymptomatic distributions.

Effects of Sex, Age, and 24-hr Volume on the Asymptomatic NBCi

Table III summarizes the effect of age, sex, and V24 on NBCi in the asymptomatic population. We included V24 as it has been

TABLE II. Descriptive Statistics of the NBCi Measurements

Variable	Sex	N	Mean	SE mean	SD	Median	Skewness
Asymptomatic							
Unrounded	F	161	0.53	0.029	0.364	0.46	1.10
	M	92	0.50	0.041	0.391	0.44	1.30
Rounded	F	161	0.13	0.031	0.392	0.00	0.84
	M	92	0.14	0.047	0.447	0.00	1.04
Combined asymptomatic							
Unrounded	F & M	253	0.52	0.024	0.373	0.45	1.16
Rounded	F & M	253	0.14	0.026	0.412	0.00	0.94
Patients							
Unrounded	F	184	1.00	0.075	1.014	0.79	3.31
Rounded	F	184	0.57	0.074	1.011	0.32	3.29

F, female; M, male; SE mean, standard error of the mean; SD, standard deviation.

TABLE III. Effect of Sex, Age, and V24 on the Asymptomatic NBCi

		P-values	
Factor	Test	Rounded	Not rounded
Sex—means	*t*	0.76	0.53
Sex—freq. dists.	χ^2	0.56	0.42
Age	Regression	0.91	0.13
V24	Regression	0.67	0.43

shown to have a strong influence on V_{max}, F_n, and V_n,[1,10,11] which are all key variables in the calculation of NBCi. As shown, there was no significant relationship between any of these potentially correlating variables and our asymptomatic subjects' NBCis. Therefore, in determining asymptomatic reference values, we can combine data from asymptomatic males and females and do not have to adjust for age and V24.

Asymptomatic Reference Values

As the NBCis are not normally distributed, confidence limits to provide cutoff values for clinical use must be obtained directly from the frequency distributions. Figure 2 shows cumulative frequency distributions of the unrounded and rounded NBCis from the asymptomatic population. Two alternative clinical cutoff points—the 90th and 95th centiles—are shown. The rounding procedure produces a distinctive "stair-step" distribution. For example, over half of the subjects (13th–65th centile) had an NBCi of zero.

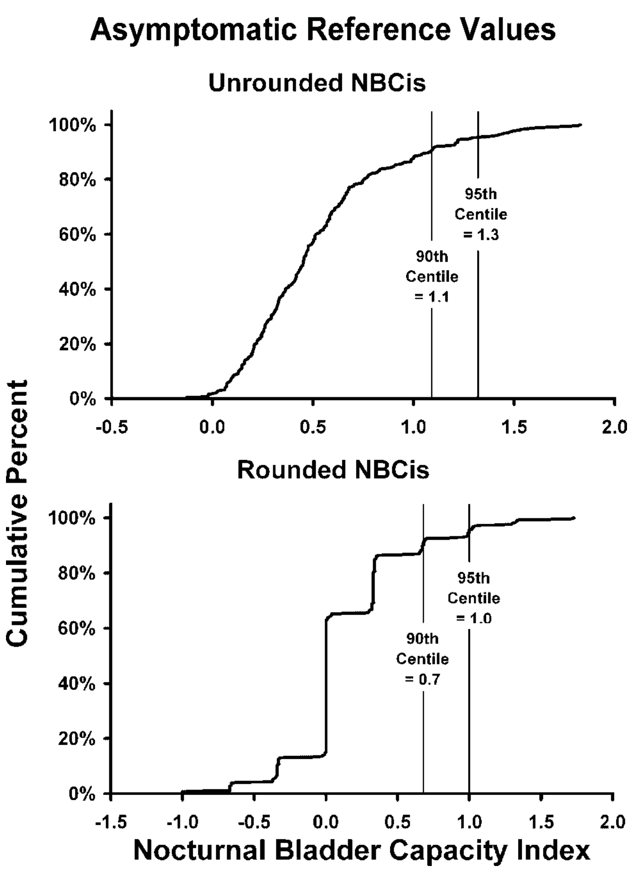

Fig. 2. Cumulative frequency distributions of unrounded and rounded NBCis from the asymptomatic volunteers.

Relationship Between Night Frequency and NBCi in the Patient Population

Among the patients, we found highly significant relationships between both the rounded ($R = 0.81$, $P < 0.0005$) and unrounded ($R = 0.86$, $P < 0.0005$) NBCis and F_n. Figure 3 shows scatter plots and regression lines illustrating these relationships.

Relative "Sensitivities" of the Rounded and Unrounded NBCis

Figure 4 plots cumulative percentages of patients with rounded and unrounded NBCis exceeding our 90th and 95th centile cutoffs versus F_n. The unrounded NBCis show a clear tendency to find more elevated NBCis among our patients than the rounded NBCis. Overall, 16% of the patients' rounded NBCis were elevated, compared to 21% of their unrounded NBCis. This difference is significant ($\chi^2 = 5.22$; $P = 0.022$).

Included in Figure 3 are dashed lines showing the 90th and 95th centile asymptomatic cutoffs. Inspection of the scatter plots in Figure 3 shows that very few patients with F_ns below 1 had NBCis above the cutoff levels, and almost all patients with F_ns above 3 had NBCis above the cutoff values—thus yielding three F_n ranges: <1, 1–3, and >3. Figure 5 plots percentages of patients in these three F_n ranges that had NBCis greater than the asymptomatic cutoffs. In the 1–3 F_n range more unrounded than rounded NBCis are above the cutoff level. This difference is particularly evident at the 90th centile cutoff.

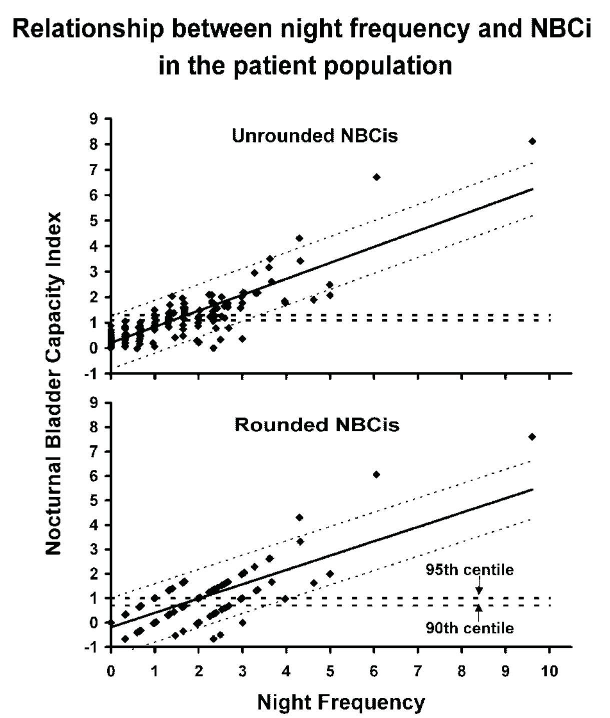

Fig. 3. Scatter-plots of the relationships between nocturnal frequency and unrounded and rounded NBCis. The 90th and 95th centile lines plot values from the cumulative frequency distributions shown in Figure 2.

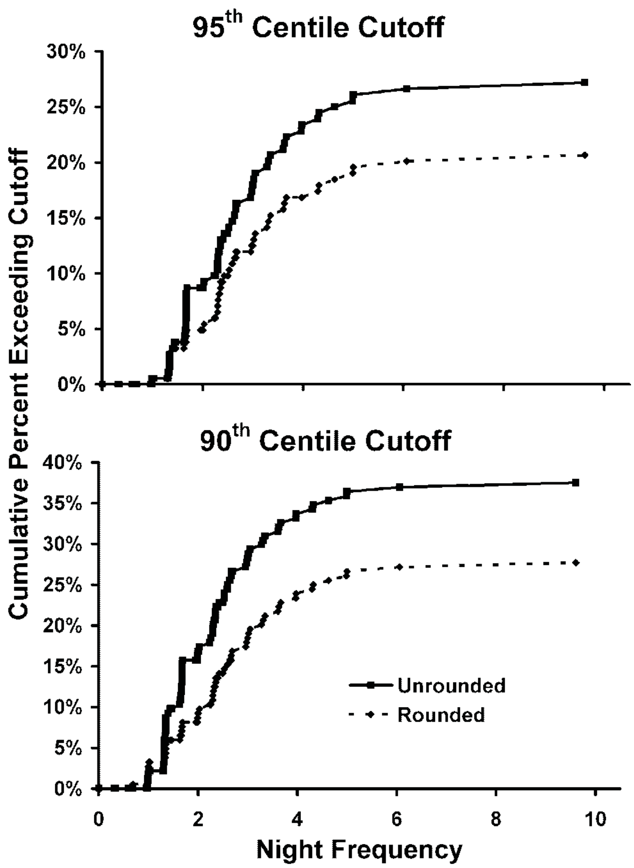

Fig. 4. Cumulative percentages of patient NBCis exceeding the 95th and 90th asymptomatic NBCi centiles from Figure 2.

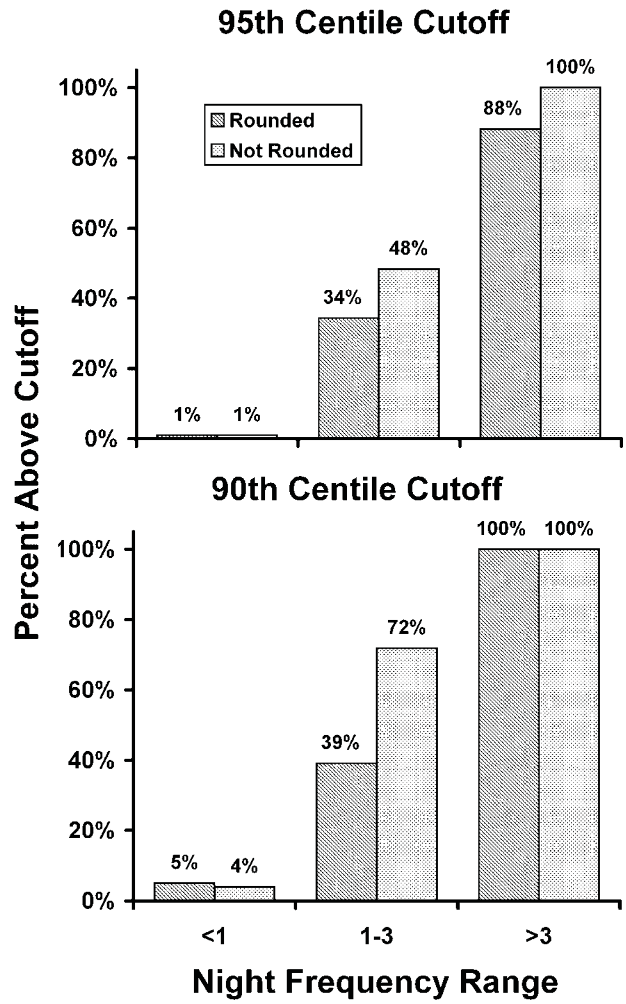

Fig. 5. Percentages of NBCis in three nocturnal frequency groups that were above the 95th and 90th centile cutoffs.

DISCUSSION

Clinical NBCi Cutoff Values

We found the following NBCi asymptomatic reference values:

95th centile : 1.3(unrounded), 1.0(rounded)

90th centile : 1.1(unrounded), 0.7(rounded)

These reference values might serve as clinical cutoff limits for the NBCi. The 90th centile cutoff values would produce 10% false positives; the 95th centile cutoff values would produce 5% false positives, but would also produce a larger number of false negatives.

Based on their study of symptomatic patients, Weiss et al.[1] suggest a cutoff of 2 as indicative of a "highly significant" NBCi. The present study's results would put a rounded NBCi of 2 at the 99.99th centile of asymptomatic volunteers. Thus, our results confirm Weiss et al.'s characterization of an NBCi > 2 as a "highly significant" indicator of low nocturnal bladder capacity. However, our results also suggest that lowering the cutoff might increase the sensitivity, with minimal effect on specificity, of NBCi as a test for low nocturnal bladder capacity.

Relationship Between NBCi and Night Frequency

We found a highly significant tendency among symptomatic patients for NBCi to increase with increasing night frequency (Fig. 3). Using our proposed 90th and 95th centile cutoffs, we also found that when $F_n > 3$, NBCi was almost always elevated, and when $F_n < 1$ NBCi was rarely elevated (Fig. 5). Therefore, we suggest that the NBCi measurement adds the most clinical information when the patient's F_n is in the 1–3 voids per night range.

Effect of Rounding on the NBCis Diagnostic Sensitivity

We found that rounding up the predicted night frequency ($V_n/V_{max} - 1$) to the nearest higher integer decreases significantly the number of patients with LUTS that have elevated NBCis. The stair-step appearance of the asymptomatic NBCi cumulative distribution is another manifestation of this insensitivity. Rounding up causes patients with very different V_ns to have the same NBCi. For example, a patient with a V_n of 550 and a V_{max} of 500 would have the same rounded-up F_{n-p} as a patient with a V_n of 950 and a V_{max} of 500.

$$550/500 = 1.1; \text{Round-up}(1.1-1) = 1$$
$$950/500 = 1.9; \text{Round-up}(1.9-1) = 1$$

This effect explains why large percentages of the asymptomatic population have the same rounded NBCi (Fig. 2).

The same effect created the "under-detection" of elevated NBCis in the patient population. Patients that had V_n/V_{max}

TABLE IV. Examples of Elevated Unrounded and "Normal" Rounded NBCis From Patients

Pt	F_n	V_n	V_{max}	$V_n/V_{max}-1$	Round-up	NBCi—rounded	NBCi—not rounded
A	2.7	721	350	$2.1-1=1.1$	2	$2.7-2=0.7$	$3.7-2.1=1.6$
B	1.5	530	500	$1.1-1=0.1$	1	$1.5-1=0.5$	$2.5-1.1=1.4$
C	1.6	531	495	$1.1-1=0.1$	1	$1.6-1=0.6$	$2.6-1.1=1.5$

ratios that were only slightly above an integer (thus requiring a large round-up) tended to have elevated unrounded NBCis and "normal" rounded NBCis. Table IV illustrates this effect in the three illustrative patients who had rounded NBCis below and unrounded NBCis above the 95th centile cutoff point. All three had V_n/V_{max} ratios (2.1 and 1.1) that were only slightly above an integer, which caused the rounding-up to greatly increase the expression $[V_n/V_{max}-1]$ thereby significantly decreasing NBCi.

Patients B and C in Table IV are far from requiring two voids to eliminate their night urine production ($V_n/V_{max}=1.1$). In contrast, the 950/500 example above illustrates a hypothetical patient who is close to requiring two voids to eliminate night urine production ($V_n/V_{max}=1.9$). Yet rounding up caused the predicted night voids of both patients to be the same. Thus, rounding up eliminates the ability of the NBCi to distinguish a patient that is very far from requiring an extra void to eliminate their night urine production from one who is very close to requiring an extra void. The data presented thus provide a rationale for eliminating rounding up the predicted number of night voids from the calculation of the NBCi.

Rationale for the Unrounded NBCi

We propose the following rationale to support the alternative unrounded NBCi calculation:

1. Instead of focusing on night frequency, focus on the number of voids required to eliminate night urine production.
2. The predicted number of voids that eliminate night production is V_n/V_{max}.
3. The actual number of voids required to eliminate night production is F_n+1. (One is added to Fn to include the first morning void in the elimination of nocturnal urine production.)
4. Therefore, the unrounded NBCi is actual-predicted voids or $(F_n+1)-V_n/V_{max}$.
5. This equation is simply a restatement of the Unrounded NBCi equation:

$$\text{Unrounded NBCi} = \text{Fn}-\left(\frac{V_n}{V_{max}-1}\right)$$

NBCi based on the elimination of night volume rationale

$$= \text{Fn}+1-\frac{V_n}{V_{max}}$$

6. It is reasonable to include fractional voids in the predicted number of voids required to eliminate a predetermined volume. The fraction can be considered an indication of how close the patient is to requiring another void to eliminate his or her night urine production.

The unrounded NBCi calculation has the added practical benefit of eliminating the round up step from the NBCi calculation—a step that not infrequently causes problems in busy clinics (Weiss, 2009, unpublished observation).

Clinical Applications

While the NBCi is useful as a measure of the contribution of diminished nocturnal bladder capacity to nocturia in individual patients, the conditions underlying low nocturnal bladder capacity are not identified by such diary analysis. The finding of low nocturnal bladder capacity should launch an attempt to explain why the patient is awakened to void at bladder volumes lower than those prompting bathroom visits in the awake state. Such underlying conditions may include administration of beta blockers just before retiring, various insomnia states and as yet uncharacterized autonomic factors that are dependent upon condition. Clearly, much work needs to be done to identify causes and corresponding therapies for low nocturnal bladder capacity.

Weaknesses of the Study

V_{max} increases with increasing diary duration,[9] and our study was limited to 3-day diaries. Therefore, our cutoff values are most accurate for 3-day diaries. Diaries shorter than 3 days will tend to produce NBCis somewhat larger than ours, and diaries longer than 3 days will tend to produce NBCis somewhat smaller than ours.

We suggest that the detection of more elevated NBCis among a patient population with LUTS indicates that the unrounded NBCi has greater diagnostic sensitivity. However, this suggestion relies on the assumption that the additional patients with increased NBCis do have reduced nocturnal bladder capacity. The alternative hypothesis, that these additional "abnormal" NBCis are false positives, is not disproven.

CONCLUSIONS

We found the following 90th and 95th centile confidence limits of rounded and unrounded NBCis from asymptomatic volunteers:

Rounded NBCi : 0.7 and 1.0
Unrounded NBCi : 1.1 and 1.3

Based on these data, and assuming the clinical standard of excluding 5% of "normals" and the greater sensitivity of the unrounded NBCi summarized below, we suggest that an unrounded NBCi of 1.3 be considered a cutoff point above which decreased nocturnal bladder capacity should be investigated as an etiologic contributor to nocturia.

The NBCi can be calculated with predicted night voids either unrounded or rounded up. We found that rounded NBCis were identical across asymptomatic subjects with widely varying V_n/V_{max} ratios; whereas unrounded NBCis varied continuously with the V_n/V_{max} ratio. We also found that the unrounded NBCi "detected" significantly more elevated NBCis among female patients with LUTS than did the rounded NBCi.

Therefore, we suggest that the unrounded NBCi be adopted as the more sensitive diary-based clinical test for reduced nocturnal bladder capacity.

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