W4: Are we meeting the needs of older people with nocturnal LUTS?

Workshop Chair: Karel Everaert, Belgium
28 August 2018 09:00 - 10:30

Start	End	Topic	Speakers
09:00	09:05	Introduction	Karel Everaert
09:05	09:25	Nocturnal LUTS, what, when, standardisation of terminology	An-Sofie Goessaert
09:25	09:45	Waking from sleep to void is not benign, focus on falls	Wendy Bower
09:45	10:05	Leg edema, obvious?	Karel Everaert
10:05	10:25	Blood Pressure and nocturnal LUTS	D Michael Whishaw
10:25	10:30	Discussion and questions are included in the above teaching sessions. Concluding remarks	Karel Everaert

Aims of Workshop
Nocturnal LUTS in older people is prevalent and bothersome symptoms however underdiagnosed. Clinicians lack confidence in how evaluating and treating the symptoms resulting in catheters and briefs. As nocturnal LUTS cannot be considered as benign a more stringent diagnostic workout is needed. Increasing clinicians their confidence will help them in starting up therapy and improving general health and comfort to patients. The focus of this workshop is improving diagnosis of nocturnal LUTS with a blink of the eye toward therapy.

Learning Objectives
- Application of the 2017 standardisation of terminology report on nocturnal LUTS and understand the gaps and restrictions in older people.
- Learn how to diagnose heart failure and explain how blood pressure can influence nocturnal urine output.
- Understand the consequences of treatment.
- Understand the different aspects of Nocturia, Falls and multi-morbidity.
- Learn to recognise heart failure in the diagnostic workout of nocturia.
- Better understand how blood pressure and edema can influence nocturnal LUTS and how this can affect the therapy.

Learning Outcomes
After the course students will be able to diagnose nocturnal LUTS in a holistic manner and start treatment with confidence.

Target Audience
Clinicians, nurses

Advanced/Basic
Advanced

Conditions for Learning
Interactive workshop restricted to 40 people. We will use modern educational techniques like microteaching and case report discussion.

Suggested Learning before Workshop Attendance
This workshop is partially based on microteaching, so reading the articles summarised below (suggested reading = must read) is mandatory for a good workshop development.

Suggested Reading
Pathophysiology of nocturnal lower urinary tract symptoms in older patients with urinary incontinence. Denys MA, Decalf V, Kumps C, Petrovic M, Goessaert AS, Everaert K. Int J Urol. 2017 Nov;24(11):808-815. doi: 10.1111/iju.13431. Epub 2017 Aug 16

Diagnosing the pathophysiologic mechanisms of nocturnal polyuria. Goessaert AS, Krott L, Hoebeke P, Vande Walle J, Everaert K. Eur Urol. 2015 Feb;67(2):283-8. doi: 10.1016/j.eururo.2014.09.003. Epub 2014 Sep 18

Nocturnal polyuria in a nursing home and effect on quality of life. Goessaert AS, Denys MA, Deryckere S, Everaert K. J Am Geriatr Soc. 2013 Oct;61(10):1812-3

Nocturia as a marker of poor health: Causal associations to inform care. Bower WF, Whishaw DM, Khan F. Neurourol Urodyn. 2017 Mar;36(3):697-705. doi: 10.1002/nau.23000. Epub 2016 Apr 6

TANGO - a screening tool to identify comorbidities on the causal pathway of nocturia. Bower WF, Rose GE, Ervin CF, Goldin J, Whishaw DM, Khan F. BJU Int. 2017 Jun;119(6):933-941. doi: 10.1111/bju.13774. Epub 2017 Feb 12.

The Nobel Prize in Physiology or Medicine 2017 for their discoveries of molecular mechanisms controlling the circadian rhythm. Jeffrey C. Hall, Michael Rosbash, Michael W. Young. https://www.nobelprize.org/nobel_prizes/medicine/laureates/2017/

The International Continence Society Standardisation of Terminology in Nocturia
Hashim Hashim, Marco Blanker, Jens Christian Djurhuus, Jane Meijlink, Vicky Morris, Peter Petros, Jian Guo Wen, Alan Wein, Marcus Drake.
https://webcache.googleusercontent.com/search?q=cache:9efsdQhX7icJ:https://www.ics.org/Documents/DocumentsDownload.aspx%3FDocumentID%3D3571+&cd=2&hl=nl&ct=clnk&gl=be

Circadian Variation in Post Void Residual in Nursing Home Residents With Moderate Impairment in Activities of Daily Living. Decalf V, Huion A, Denys MA, Kumps C, Petrovic M, Everaert K. J Am Med Dir Assoc. 2017 May 1;18(5):433-437. doi: 10.1016/j.jamda.2016.11.022. Epub 2017 Jan 17.

Handouts:

Nocturnal LUTS, what, when, standardisation of terminology
An-Sofie Goessaert

In this part, we will discuss the current terminology regarding nocturnal LUTS applied on older patients, based on the ICS report on the terminology for nocturia and nocturnal lower urinary tract function of 2018. (1)
Nocturia can be looked at as a sign (a term that applies to an objective observation apparent to the patient, physician and others; this can include observations from a frequency voiding chart, questionnaire, etc.), a condition (defined by the presence of urodynamic observations associated with characteristic signs and symptoms and/or non-urodynamic evidence of relevant pathologies), or a symptom (any subjective evidence of disease apparent to the patient).
The current definition of nocturia is “waking to pass urine during the main sleep period”. Although this definition has changed recently (no mention of “each void being preceded and followed by sleep), making it more clinically applicable, this definition does not take bother into account and therefore might select patients who do not consider their nocturia as bothersome. Also, in an older population, where the prevalence of nocturia (1x) goes up to 70%, one can wonder if nocturia should be considered as a pathological sign, condition or symptom rather than an aging proces.
Nocturia is a multifactorial condition, it can be based on reduced bladder capacity, nocturnal polyuria or 24hr polyuria. With aging, it is known that the bladder capacity decreases dues to change in collagen-muscle ratio and increased fibrosis. (2) Due to a loss of circadian rhythm of hormones such as vasopressin, nocturnal polyuria can also be considered a consequence of aging to certain extent. Also underlying factors for development of nocturnal polyuria, such as peripheral edema and hypertension have a higher prevalence with aging. (3) The ICS definition of nocturnal polyuria is “excessive production of urine during the individual’s main sleep period”. The former definition assumed an increased urine production during a night of 8 hours. However, duration of sleep is highly variable, not only inter- but also intra-individually. Besides, sleep quality and duration changes with age, so a fixed time frame was debatable. With the current definition the meaning of “excessive” urine production is not defined, as there are many different ways to classify nocturnal polyuria depending on the clinical or research setting.
As there have been made considerable changes to the definitions that are not yet common knowledge, these changes will be discussed based on the case of an older patient suffering from nocturnal lower urinary tract symptoms.

(1) Hashim H. et al. ICS Report on the terminology for nocturia and nocturnal lower urinary tract function. 2018. Not yet published
(2) Suskind A. Curr Bladder Dysfunct Rep. 2017; 12(1): 42-47. The aging overactive bladder: a review of aging-relatd changes from the brain to the bladder
(3) Denys M. et al. Int J Urol. 2017; 24 : 808-815. Pathophysiology of nocturnal lower urinary tract symptoms in older patients with urinary incontinence.

Waking from sleep to void is not benign, focus on falls
Wendy Bower

How are falls related to nLUTS?
The temporal relationship of falls and nocturia has been poorly investigated. Patients with nocturia have a markedly increased risk of injurious falls compared to people who sleep through the night (OR 2.2 for any fracture, 1.4 for hip fracture) (1). Nocturia can fluctuate night to night (2). This is likely due to changes in medical status and fluid displacement.

Patients who fall in hospital are more likely to have a longer stay and display reduced confidence and functional ability on discharge (3). An Australian study showed that more in-hospital falls occurred between 2 and 4am than at any other time interval, mostly in the patients’ bedrooms or en route to the toilet. A recent Belgian audit in the aged care context suggested

that at least 36% of all falls are related to toileting. Of these falls, 75% occurred during the night. Clearly falling may be related to nocturia.

It may be that people make extraordinary efforts to avoid an incontinent episode, including placing themselves at increased risk of falling. More likely, the common causal link between voiding at night and falling is multifactorial and includes frailty, multimorbidity, polypharmacy or cognitive and gait changes seen on awaking unrefreshed or from insufficient sleep (4).

Look for nLUTS in a person at high risk of falls

The multi-factorial presentation of illness impacts the range of incontinence and bladder problems. Our experience is that patients admitted to hospital wards are generally screened for incontinence and the need for assistance with toileting but not specifically for bladder symptoms at night. First line intervention for nocturnal lower urinary tract symptoms while hospitalized is not standard. Pads are commonly used even for patients who have nocturia but are not incontinent (5).

The various Falls Risk tools screen for generic elimination symptoms but do not necessarily differentiate between occurrence during the day or night (e.g. Falls Risk Assessment and Management Plan asks about constipation, urinary or faecal frequency or urgency or nocturia in a single question). Some protocols support prevention of falls by suggesting that patients be woken every two hours to check whether they need help toileting.

Impact of sleep parameters on falls risk and nLUTS

One of the main drivers of nocturia is an increase in nocturnal diuresis. This can reflect a disorder of solute or free water excretion, systemic illness, injury-related oedema or result from an acute condition (6,7). Waking after a short time asleep is associated with impaired standing balance and step length when walking; changes which are a risk for falls and not corrected by adequate lighting (8).

Deterioration of the sleep-wake cycle and sleep disruption (irrespective of the cause) can itself induce nocturnal polyuria (9). The sleep disturbance associated with nLUTS contributes to poor in-hospital outcomes, increases the risk of falls and fracture and adds considerably to health care resource use. Decreasing nocturia by even one episode per night can result in improved restorative sleep, increased safety at night, reduced daytime fatigue and earlier return to health (10).

References

1. Damian J et al. Factors associated with falls among older adults living in institutions. BMC Geriatrics. 2013, 13(1):13-19.
2. van Doorn B et al. Once nocturia, always nocturia? Natural history of nocturia in older men based on frequency-volume charts: the Krimpen study J Urol. 2011, 186(5):1956-61
3. von Renteln-Kruse W et al. Fall events in geriatric hospital in-patients. Results of prospective recording over a 3-year period. Zeitschrift fur Gerontologie und Geriatrie. 2004, 37(1): 9-14
4. Gibson W et al. The association between lower urinary tract symptoms and falls: Forming a theoretical model for a research agenda. Neurourol Urodyn. 2018, Vol.37(1):501-509
5. Sacco-Peterson M et al. Struggles for autonomy in self-care: the impact of the physical and socio-cultural environment in a long-term care setting. Scand J Caring Sci. 2004, 18(4):376-86
6. Nakagawa H et al. Impact of nocturia on bone fracture and mortality in older individuals: a Japanese longitudinal cohort study. J Urol. 2010, 184(4):1413-8
7. Bing MH et al. Nocturia and associated morbidity in a Danish population of men and women aged 60-80 years. BJU Int. 2008, 102(7):808-14.
8. McBean AL et al. Standing Balance and Spatiotemporal Aspects of Gait Are Impaired Upon Nocturnal Awakening in Healthy Late Middle-Aged and Older Adults. J Clin Sleep Med. 2016;12(11):1477-1486.
9. Kamperis K et al. Excess diuresis and natriuresis during acute sleep deprivation in healthy adults. Am J Physiol Renal Physiol. 2010, 299(2):F404-11.
10. Bliwise DL et al. Delay of first voiding episode is associated with longer reported sleep duration. Sleep Health. 2015, Sep;1(3):211-213.

Leg edema, obvious?

Karel Everaert

Prescriptions for nocturia are given in progressively more frequent older people with rising safety concerns. Even though medication becomes safer (low dose, gender specific), a certain risk has to be dealt with. This might become a problem for surgical disciplines (Urology, Gynaecology) who treat most of the nocturia patients as they are not used to diagnose the comorbidities related to an increased risk of hyponatremia. Some basic knowledge of leg edema and heart failure is a strong example and actually little knowledge is needed to increase the feeling of safety for the clinician and actual safety for the patient.

Edema and specially leg edema causes nocturnal polyuria and nocturia through resorption of the fluid when supine resulting in an immediate excess in urine output and a delayed increase in ANP related salt diuresis. Combining water retention due to desmopressin and increasing salt loss due to these comorbidities, explains the increased risk for complications like hyponatremia. Leg edema are seen with liver, heart or kidney disease or following varices of the legs, lack of physical activity or muscle paralysis. Concomitant medication that can cause edema are antidepressants (MOA-inhibitors), antihypertensives (mainly Calcium channel blockers), antivirals, chemotherapeutics, cytokines, hormones (sex hormones and glucocorticoieds) and NSAID. Diagnosis is based on expert opinion rather than science and the available guideline documents do not mention nocturia. Heart failure has to be suspected when there is a history of heart disease, when edema and/or weight gain with rapid onset is, excertional dysnpea or orthopnea. Normal serum BNP concentration rules out uncontrolled heart failure. Desmopressin for nocturia is contraindicated in patients with congestive heart failure (New York Heart Association Class II to IV) or uncontrolled hypertension and should be used with caution (e.g., monitoring of volume status) in patients with New York Heart Association Class I congestive heart failure because of the risk of fluid overload and electrolyte abnormalities, patients with heart failure may also be at increased risk for low sodium concentrations.

Leg edema due to varicose veins or lack of physical activity (elderly, wheelchair bound patients) can be prevented with stockings or treated with pressotherapy or daytime diuretics and leg elevation with low levels of evidence and certain complications like pressure sores and discomfort. Drug induced edema can be treated by switching medication.
Conclusion: some basic knowledge of leg edema, its causes and its diagnosis is needed to treat nocturia in older people. The diagnosis is based on history taking, physical examination (pitting edema, blood pressure if not known) and serum analysis (creatinine, sodium, liver tests, osmolality and BNP) and is perfectly possible within a surgical consultation.

References

1) The Criteria Committee of the New York Heart Association. (1994). *Nomenclature and Criteria for Diagnosis of Diseases of the Heart and Great Vessels* (9th ed.). Boston: Little, Brown & Co. pp. 253–256.
2) 2016 European Guidelines on cardiovascular disease prevention in clinical practice. Piepoli MF et al. Eur J Prev Cardiol. 2016, 23(11):NP1-NP96.
3) Edema: Diagnosis and Management. KATHRYN P et al. Am Fam Phys, 2013, 88; 2: 102-13
4) Treatment of Edema. JAMES G. O'BRIEN et al. Am Fam Phys, 2005, 71; 11: 2111-7

Blood Pressure and nocturnal LUTS

Michael Whishaw

Systemic disease

Voiding at night is a common symptom of systemic disease. For example, nocturia is seen with poorly controlled diabetes, impaired circulation, congestive heart failure, hypertension, metabolic syndrome, anxiety and autonomic dysfunction, airway occlusion during sleep and renal and malignant disease (Bower 2016). The final common pathway is usually increased urine production during the night (nocturnal polyuria – NP) due to a change in vascular resistance, clearance of third space fluid or osmotic or free water diuresis. Intrinsic is the absolute, and variable level of blood pressure.

Hypertension

Hypertension per se is associated with nocturia with an OR 1.30-2.68 in those with at least 2 voids per night, with a significant association in 11 of 14 identified studies in a systematic review.
There is a small amount of evidence that hypertension may be independently associated with nocturia in the absence of any co-existent morbidity (Victor 2017), although there is likely to be some contribution to NP as a side-effect of the BP drugs. The link is multifactorial, including effect on glomerular filtration, and hormonal mechanisms including the renin-angiotensin-aldosterone system. In most cases of NP in hypertensives though, there will be a contribution from a co-existent comorbidity

Non-dipping and nocturnal hypertension

It is normal for nocturnal BP to drop by at least 10% (a circadian rhythm). A drop of less than 10% is referred to as a "non-dipping" BP profile or non-dipping hypertension. It may occur in many conditions, and is commonly associated with NP. The corollary also holds in that nocturia is associated with higher nocturnal systolic BP, and lower dipping (Obayashi 2015).
A higher than normal nocturnal BP is understood to result in NP through heightened renal perfusion. Non-dipping hypertension occurs in about 25% of hypertensives and is probably associated with renal disease progression, greater end-organ damage and increased cardiovascular morbidity (Pickering 2001).

Related to this, nocturia is an independent predictive factor of prevalent hypertension in obstructive sleep apnoea (Destors 2015). What is more, morning hypertension may predict sleep disordered breathing - SDB (Hongyo 2016).

SDB is usually best managed with CPAP. Otherwise non-dipping hypertension should be treated with carefully tailored hypotensive therapy.

Orthostatic hypotension

Orthostatic (postural) hypotension is a feature of autonomic dysfunction, seen in a number of conditions including Parkinson's Disease. The postural hypotension limits renal perfusion in the upright state, which then increases sometimes markedly when assuming the supine state at night and resulting in NP. A case presentation will highlight how challenging this can be to treat effectively.

Hypertensive drugs

Drugs to treat hypertension may cause NP through different mechanisms including postural hypotension. Calcium blockers, especially amlodipine, may cause fluid retention with peripheral oedema. Thiazide diuretics have 24 hour action promoting a small nocturnal diuresis.

References

1. Bower WF, et al. Nocturia as a marker of poor health: Causal associations to inform care. Neurourology and Urodynamics. 2017 Mar 1; 36(3):697-705.
2. Victor RG, et al. Nocturia as an Unrecognised Symptom of Uncontrolled Hypertension in Middle-age Black Men. Hypertension. 2017, 70(Suppl 1)
3. Obayashi K, et al. Independent Associations Between Nocturia and Nighttime Blood Pressure/Dipping in Elderly Individuals: The Heijo-KYO Cohort. Journal of the American Geriatrics Society. 2015, 1;63(4):733-8.
4. Pickering TG, et al. Nocturnal non-dipping: What Does it Augur? Current Opinion in Nephrology and Hypertension. 2001, 1;10(5):611-6.
5. Destors M, et al. Nocturia is an Independent Predictive Value of Prevalent Hypertension in Obstructive Sleep Apnoea Patients. Sleep Medicine. 2015, 16:652-658
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ICS workshop

Nocturnal LUTS, what, when, standardization of terminology

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An-Sofie Goessaert

Affiliations to disclose[†]:

none

† All financial ties (over the last year) that you may have with any business organization with respect to the subjects mentioned during your presentation

Funding for speaker to attend:

- [ ] Self-funded
- [ ] Institution (non-industry) funded
- [x] Sponsored by: *Astellas*

CASE

Female, 78 years old

Medical history: diabetes mellitus type II, arterial hypertension

Problem: fall during nocturnal toilet visit, urological work-up to prevent future nocturnal falls

History: nocturia 3-4x, high voiding frequency during daytime; urinary incontinence from time to time

Terminology

Symptom:

Any morbid phenomenon or departure from the normal in structure, function or sensation, experienced by the person and indicative of disease or a health problem.

Symptoms are either volunteered by, or elicited from the person or may be described by the person's caregiver

ICS report on the terminology for nocturia and nocturnal lower urinary tract function – Haeblin Haelin et al. – draft document www.ics.org/documents

CASE

Symptom:

- Nocturia

Terminology

Symptom case:

- Nocturia:
  - 2010: complaint of interruption of sleep one or more times because of the need to micturate. Each void is preceded and followed by sleep
  - 2018: waking to pass urine during the main sleep period

Nocturia

Changes:

- No longer defined as a "complaint" (getting up once may not be bothersome)
- With the new definition following is included:
  - Patients who need to void multiple times in the night after falling asleep, often several times in a row, and may not be able to get back to sleep again
  - Patients whose bladder does not empty fully and who consequently need to void again soon
  - Patients who suffer from insomnia or difficulty in sleeping from causes other than their bladder problem
  - Patients who wake up and then are unable to sleep due to painful or oversensitive bladders

CASE

Urinalysis: negative

Abdominal ultrasound: normal kidneys, normal bladder wall, no lithiasis, no renal or bladder masses

Postvoid residual (ultrasound): 20ml

CASE

- Daytime frequency: 8x
- Nocturia episodes: 3x
- Maximum voided volume: 160ml
- 24h urine volume: 840+320 = 1160ml
- Nocturnal urine volume: 320ml
- NPI 28%
- NI: 320/160=2

Hour	Voided volume	Incontinence
7:30 AM	120ml	++
10:15 AM	100ml	
11:25 AM	130ml	
2:30 PM	160ml	+
4:15 PM	100ml	
7:55 PM	120ml	
10:30 PM	110ml	
1:35 AM	100ml	
3:10 AM	80ml	
5:40 AM	70ml	
6:30 AM	70ml	

Terminology

Sign:

Any abnormality indicative of disease or a health problem, discoverable on examination of the patient; an objective indication of disease or a health problem. These can be quantified by a questionnaire or bladder diary

CASE

Sign:

- Nocturia

Terminology

Sign case:

- Nocturia:
  - 2010: not specifically defined
  - 2018: the number of times an individual passes urine during their main sleep period. This is derived from the bladder diary
- Measurement of the frequency of nocturia begins after sleep and concludes before the first void following intention of getting up for the day

Terminology

Other signs assessed with bladder diary or frequency volume chart:

- Nocturnal urine volume
- 24-hour voided volume
- 24-hour polyuria

Terminology

Other signs assessed with bladder diary or frequency volume chart:

- Nocturnal urine volume:
  - 2010: cumulative urine volume from voids after going to bed with the intention of sleeping to include the first void at the time of waking with the intention of rising (excludes last void before sleep)
  - 2018: total volume of urine produced during the individual's main sleep period including the first morning void
- Best to advise individuals who are filling out a bladder diary or FVC to void before going to sleep to make assessment of volumes passed easier by the healthcare provider

Terminology

Other signs assessed with bladder diary or frequency volume chart:

- 24-hour voided volume:
  - 2010: summation of all urine volumes voided in 24 hours
  - 2018: total volume of urine passed during a 24-hour period excluding the first morning void of the period; the fist void after rising is discarded an the 24-hour period begins at the time of the next void and is completed by including the first void, after rising, the following day
- No longer confusion with regard to when the 24-hour period begins and when it ends

Terminology

Other signs assessed with bladder diary or frequency volume chart:

- 24-hour polyuria:
  - 2010: excessive excretion of urine resulting in profuse and frequent micturition. It has been defined as over 40ml/kg body weight during 24 hours or 2,8l urine for an individual weighing 70kg
  - 2018: the previous definitions have not been changed
- no new research or information on defining polyuria
- Volumes passed daily vary considerably, and are influenced by environmental, physiological and pathological factors, and the amount of fluid intake

CASE

Based on the results:

- Diagnosis: Nocturia due to small bladder capacity/overactive bladder

CASE

Female, 78 years old

Medical history: diabetes mellitus type II, arterial hypertension

Problem: fall during nocturnal toilet visit after urinary incontinence episode, urological work-up to prevent future nocturnal falls

History: 2-3 nights per week nocturnal urinary incontinence, large volumes; if no incontinence at night, large voided volumes in the morning

CASE

Symptoms:

- Enuresis
- Nocturnal Polyuria

Terminology

Symptoms case:

- Enuresis:
  - 2010: complaint of involuntary loss of urine which occurs during sleep
  - 2018: complaint of intermittent incontinence that occurs during periods of sleep; if it occurs during the main sleep period, then it could be qualified by the adjective « nocturnal »*

*nocturnal: refers to « done, occurring, or active at night »

Enuresis

Changes:

- Previously believed to be a complete emptying of the bladder, later identified as both complete and incomplete emptying of the bladder
- Previously wetting in discrete portions while asleep after the age of five
- Changed to be consisted with the ICCS definition

Terminology

Symptoms case:

- Nocturnal polyuria:
  - 2010: not defined as a symptom
  - 2018: passing large volumes of urine at night
- Previously only considered as a sign, however, patients can report passing large volumes of urine at night, especially relative to the day

CASE (ambulatory)

- Daytime frequency: 5x
- Nocturia episodes: 0x
- Maximum voided volume: 570ml
- 24h urine volume: 1250ml
- Nocturnal urine volume: 570ml + ??
- NPI at least 46%

Hour	Voided volume	Incontinence
7:30 AM	200ml	+
2:30 PM	120ml	
7:55 PM	250ml	
10:30 PM	110ml	
3:10 AM		++
6:30 AM	570ml	

CASE (hospitalisation)

- Daytime frequency: 5x
- Nocturia episodes: 0x
- Maximum voided volume: 570ml
- 24h urine volume: 1430ml
- Nocturnal urine volume: 570ml+280ml=850ml
- NPI 59%

Hour	Voided volume	Residual volume	Incontinence volume
7:30 AM	200ml	80ml	
2:30 PM	120ml	130ml	
7:55 PM	250ml	90ml	
10:30 PM	110ml	110ml	
3:10 AM			280ml
6:30 AM	570ml	10ml	

CASE

Signs:

- Enuresis
- Nocturnal Polyuria

Terminology

Signs case:

- Enuresis
  - Not defined as a sign in previous terminology documents
  - 2018: « wetting » while asleep

Terminology

Signs case:

- Nocturnal Polyuria:
  - 2010: excess (over 20-30% - age dependent) proportion (nocturnal voided volume/total 24hr voided volume x 100%) occurs at night (or when patient is sleeping)
  - 2018: excessive production of urine during the individual's main sleep period. The definition used to quantify 'excessive' will need to be highlighted in both clinical and research settings and derived from a bladder diary.

Nocturnal Polyuria

Changes:

- Numerous ways of classifying nocturnal polyuria:
  - Congestive heart failure
  - Diabetes mellitus
  - Obstructive sleep apnoea
  - Peripheral oedema
  - Excessive night-time fluid intake
  - Abnormality in nocturnal secretion or action of arginine vasopressin
  - Oedema-forming states (heart failure, chronic renal disease, liver failure)
  - Autonomic nervous system dysfunction, Alzheimer's disease, multisystem atrophy, stroke, parkinsonism
  - "normal aging

Nocturnal Polyuria

Changes:

- Regardless of what definition is applied, the diagnosis of NP includes a differential diagnosis of following causes:
  - Congestive heart failure
  - Diabetes mellitus
  - Obstructive sleep apnoea
  - Peripheral oedema
  - Excessive night-time fluid intake
  - Abnormality in nocturnal secretion or action of arginine vasopressin
  - Oedema-forming states (heart failure, chronic renal disease, liver failure)
  - Autonomic nervous system dysfunction, Alzheimer's disease, multisystem atrophy, stroke, parkinsonism
  - "normal aging

CASE

Based on the results:

- Enuresis due to overdistension of the bladder with overflow + reduced bladder sensation
- Further exploration underlying causes of nocturnal polyuria

CASES background

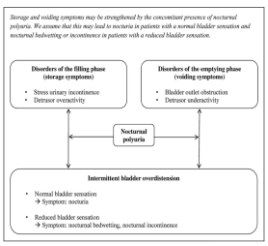
Symptoms as nocturia, frequency and urinary incontinence

- typically attributed to underlying detrusor overactivity
- can also be the result of bladder outlet obstruction, detrusor underactivity, nocturnal polyuria and loss of bladder sensation

>> all conditions that occur more frequently with increasing age

CASES background

Abnormal filling or emptying of the bladder can be linked to intermittent overdistension of the bladder, especially in older patients with nocturnal polyuria



CASES background

Detrusor underactivity is not necessarily caused by a diminished detrusor contractility, but can also be the result of dysfunctional processing of afferent information from the filling bladder, with a diminished bladder sensation

>> typically seen in patients with diabetes mellitus, an age-associated disease

CONCLUSION

Term	Definition
Enuresis	- *Symptom:* complaint of intermittent incontinence that occurs during periods of sleep - *Sign:* « wetting » while asleep
Nocturia	- *Symptom:* waking at night to pass urine - *Sign:* the number of times an individual passes urine during their main sleep period; should be quantified using a bladder diary
Nocturnal polyuria	- *Symptom:* passing large volumes of urine at night - *Sign:* excessive production of urine during the individual's main sleep period; should be quantified using a bladder diary
Nocturnal urine volume	- *Sign:* total volume of urine produced during the individual's main sleep period; should be quantified using a bladder diary
24-hour voided volume	- *Sign:* total volume of urine passed during a 24-hour period excluding the first morning void of the period; should be quantified using a bladder diary

CONCLUSION

Using a standardized terminology is important both clinically and in research

In older people it is not always easy to get a correct view on the symptoms and signs (unreliable history / voiding diary), which might have implications on treatment

In case of doubt regarding nocturnal LUTS, hospitalisation to get a good frequency-volume chart can be helpful

Thank you!

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FALLS AND NOCTURNAL LUTS

Workshop 4 ICS 2018

Wendy Bower FACP, PhD

THE UNIVERSITY OF MELBOURNE

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GHENT UNIVERSITY

Wendy Bower

Affiliations to disclose†:

Ferring Australia

Ferring International

Funding for speaker to attend:

† All financial ties (over the last year) that you may have with any business organisation with respect to the subjects mentioned during your presentation

- ☐ Self-funded
- ☐ Institution (non-industry) funded
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Falls ∞ nLUTS

= intersection of ageing and co-existing disease

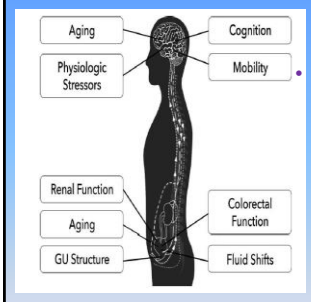
= vulnerabilities versus reserves

Common Geriatric Syndromes*

- Delirium (cognitive issues)
- Sleep and circadian rhythm
- Falls
  - 1:3 >65 yrs fall once/ year
- Urinary incontinence (Vaughan et al 2018)
  - complete and irreversible
  - ranked least important by physicians, nurses and nursing executives
- Interact with each other; common comorbidities

Bidirectional relationship: disease & bladder function

* Interfere with ADL, ↓life expectancy



Vaughan et al. J Am Geriatr Soc 66:773–782, 2018

UI: Vulnerabilities?

- Neurological: innervation, sensory dysfunction
- CVD: oedema; NP; white matter; hypertension, oxidative stress
- DM: UAB; polyuria; sensory changes
- Obesity: UUI; SUI
- Vascular: change in blood flow to bladder and brain

nLUTS

- Multiple interacting contributing conditions
  - Mobility limitations
  - Bladder changes
  - Physiological redundancy
  - Circadian rhythm disruption
  - Sleep disturbance
  - Cognitive changes
  - Acute disease and pharmacotherapy
  - Other Geriatric Syndromes

➲exacerbates impaired detrusor innervation, function and control + NUV and sleep changes

Nocturnal influences

- Ageing kidneys (Andersson 2017)
  - ↓ creatinine clearance
  - ↓ response to ADH
  - low aldosterone → Na wasting
  - ↑ rate of nocturnal urine production
    - ± extremity oedema / DM / non-dipping hypertension
- Sleep disturbance → excess diuresis (Mahler & Kamperis 2012)
- Balance and gait impairments significantly and independently associated with urgency UI (Fritel 2013)
  - Standing balance and step length ↓ after arousal from SW sleep (McBean 2016)

Balance

- Static vs Dynamic: leg strength important
  - 7.5 weaker dorsiflexors in fallers vs non fallers
  - Weak leg muscles= slower speed, > tripping
- Systems
  - Visual: environment, location, direction, speed
    - Age → loss of spatial information, depth perception and peripheral vision
  - Vestibular: information about head movement
    - Age → loss of sensory cells
  - Somatosensory: body contact and position
    - Age → ↓ cutaneous sensation
- Fear of falling changes posture: to protect head
  - Avoid movement → weakness, inefficient gait

Falls in the community

N=92,660 Korean men; slip / fall over last 1 year (Kim 2017)

- Falls prevalence 14.6%
- OR falls in elderly adults significantly ↑ in all age groups as the frequency of nocturia ↑
  - AOR 1.26 n=1 [1.12±1.41]
  - AOR 1.36 n=2 [1.20±1.54]
  - AOR 1.34 n=3 [1.15±1.56]
  - AOR 1.59 n=4 [1.29±1.95]
  - AOR 1.73 n= 5 [1.41±2.11]

Falls in the community

- Excessive Daytime Sleepiness (using ESS) (Hayley et al 2015)
  - Signif ↑ risk of falls both genders
  - Signif assoc nocturia and EDS (F: p<0.03; M p< 0.01)
- Medication use and falls
  - 25% in no medications group
  - 48% in x5 medication group (Blake 1988)
  - Diuretics 3x more common in fallers than non fallers
  - Mechanisms: dizziness, confusion, withdrawal insomnia, ataxia, reversible dementia, ↓ blood pressure
- Environment, footwear and non-use of prescription glasses

Nocturia, Falls and Mortality in elderly

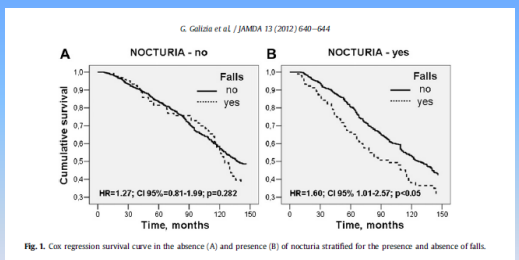


Fig. 1. Cox regression survival curve in the absence (A) and presence (B) of nocturia stratified for the presence and absence of falls.

Nocturia & falls: HR 1.6 (1.01-2.57)
No nocturia and falls: HR 1.27 (-.81-1.99) (Galizia 2012)

Esther: 84 year old female

Med History:
- Normal pressure hydrocephalus; shunt off
- IHD; dyslipidaemia; AF
- Depression
- GORD
- Previous SDH
- Asthma
- RUTI
- Unilateral knee pain
- SDB

Falls risk high
- Dizzy, impulsive, tired
- 4 wheel frame
- Lives alone
- X5 admissions for a fall

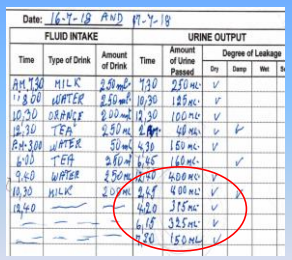
LUTS
- N=8 last 1 year
- NP
- UUI with standing up
- Day frequency 7-9
- SUI with cough
- Nil PVR
- Recent fall at night – family "forbidden" night toileting

UDI // DO, SUI, no DV or BOO

Falls as a GS: at least 3/ month or the fear of falling prevents regular activities

Esther in the Hall with UI

- FVC: NUP1600mL; day VV<200mL
- Sleeps 9 hours
- FUST 2 hours



Date: 16-7-18 AND 17-7-18

FLUID INTAKE			URINE OUTPUT				
Time	Type of Drink	Amount of Drink	Time	Amount of Urine Passed	Degree of Leakage		
					Dry	Damp	Wet
AM 7.30	MILK	250 mL	7.30	250 mL	✓		
11.00	WATER	250 mL	10.30	125 mL	✓		
10.30	ORANGE	200 mL	12.30	100 mL	✓		
12.30	TEA	250 mL	2 PM	40 mL	✓	✓	
PM 3.00	WATER	50 mL	4.30	150 mL	✓		
6.00	TEA	250 mL	6.45	160 mL		✓	
9.40	WATER	250 mL	9.40	400 mL	✓		
10.30	MILK	200 mL	2.45	400 mL	✓	✓	
12.40			4.20	375 mL	✓		
			6.15	325 mL	✓		
			7.30	150 mL	✓		

Points of dysfunction → nLUTS

- Afferent information
  - Late sensation; ? white matter disease
- Reception and integration of CNS information
  - Cognitive changes
- Appropriate efferent output
  - Lumbar spine narrowing; sciatic nerve compression
- Mobility
  - ↓gait speed;↓ stride length; wider base of support;
  - Requires gait aid; wears glasses
- End-organ ability to respond
  - OAB; blood flow changes; post-UTI inflammation
- Other age-related change
  - ADH; small capacity bladder

How likely do you consider the following causes of nLUTS?

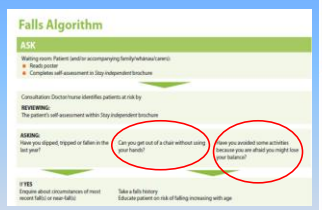
- Geriatric syndrome UI
  - ? complete and irreversible
- OAB: hypoperfusion, hypoxia and oxidative stress
- Geriatric syndrome SCR / Sleep disorder / Falls
- Idiopathic nocturnal polyuria (NP)
- NP related to cardiovascular condition
- Pain from knee and lumbar spine
- Frailty

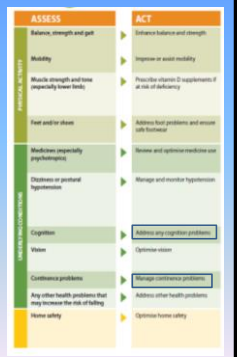
Which diagnostic evaluations?

- Extensive clinical examination
- Cause of dizziness
- Pain management
- Sleep study
- Estimate of NUV
- Falls and Balance evaluation

Falls review

(NZ Falls Toolkit Algorithm)





Appropriate treatment options?

- Adaptive resrves?
- Treatment of
  - Sleep disordered breathing
  - Mobility and balance
  - Voiding mechanics
  - OAB: Bladder training and beta 3 agonist
  - PFM rehabilitation for SUI
- " For most geriatric syndromes single-component interventions are less effective than multicomponent interventions…"
  (Vaughan et al 2018)

In-Hospital Falls

- Multifactorial
- Associated with comorbidities, function and cognition (Lim 2018)
- Older patients have a poor recognition of their own falls risk (Lim 2018)
  - 18% under-aware
  - 51% over-estimate risk
- Falls risk factors
  - Age & gender
  - History of falls
  - Slow gait ± poor balance
  - Muscle weakness
  - Dizziness
  - Vision limitation
  - Medication for DM, epilepsy, mood/ behaviour
- Significant predictor: benzodiazepine within 12 hours (Domingue et al 2018)

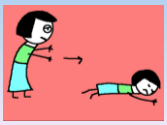
In-patient falls

- Incidence: 3.1-6.1 / 1000 patient days
- Falls in hospital →
  - longer admission
  - ↓ confidence
  - ↓ function at discharge
  - ↑ healthcare needs (Morello 2015)

- Severity of injury unrelated to falls risk classification
- After CVA 46% chance of falling in hospital

Falls during Night

- 32% of falls (127/402 incidents)
- Falls related to toileting
  - Belgium: 36%; Australia: 34%
  - No category for falls related to toileting (RiskMan)
- Falls related to toileting at night
  - Australia 15% all falls; Belgium: 27%
  - 46% all night falls
- Night toileting falls injuries
  - 22/59 no harm
  - 34/59 minor injuries
  - 3/59 fractures (5%)



Toilet-related falls at night

- Most falls 23:00-23:59hrs or 5:00-5:59hrs
- Toileting–related night falls:
  - Half occur before 1am
  - *most Nocturnal Polyuria within 2-3 hours of sleep
- Location of toileting–related night falls
  - 46% bedside
  - 27% in bathroom
  - 20% in middle of room
- Activity before toileting–related night fall
  - 36% going to toilet
  - 32% getting out of bed
  - 10% returning from toilet

Toileting–related Falls at night (RMH)

- 88% in patients not considered independent
- 80% patient not using recommended assistance level
- 90% ✓Falls Risk Management Plan
  - 48% no strategies selected
  - 48% "encouraged to use bell for toileting"
- Diagnoses and co-morbidities
  - 58% cognitive compromise
  - 19% using diuretics at time of fall
  - LL fracture 17%; delirium /dementia 8.5%

Esther in the Hospital

- Admitted for rehab
- Fall in bathroom
  - 12.30am
  - Lost balance; hit head
  - En route to toilet
  - Dizzy at the time
  - Using frame; no assistance requested
  - Lacerations and rib pain
- Associated factors
  - Early sleep disruption
  - Effort to avoid incontinence
  - Cognition
  - Strength
  - Emotional state
  - Motivation
  - Nutrition
  - Sleep
  - Medication
  - Health attitude
  - Communication

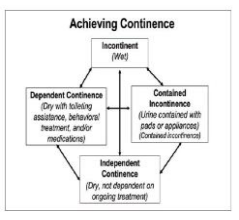
Is in-patient management different?

- Overactive bladder
- Dizziness
- Sleep disorder
- Nocturnal polyuria
  - NUV; type of diuresis; ? related to CVD / shunt / ankle
  - Intervention
- Other?
  - Individualised care plan for toileting
  - Sleep strategies: reduce disturbance

Is in-patient management different?

First treat

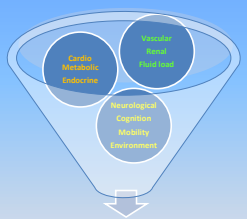
- Environmental factors
- Unmanaged medical issues (dizziness, DO, shunt)
- Modifiable factors
  - Immediate (sleep, SDB, pm plan)
  - Longer term (CVD, NP)
  - Multidisciplinary input
- Post -discharge referral
  - Falls, Continence, Sleep services



Gaps in Evidence

- Unclear how to evaluate types of nLUTS
  - Is overflow UI back?
  - Does type of incontinence change management?
- No current treatment algorithms for nLUTS
  - In-patients & community dwelling older people
  - Which system / comorbidities to target first?
- Awaiting trials of multicomponent therapies

Summary: Falls and nLUTS bi-directional



UI and nLUTS in older people

Leg Oedema, Obvious?

Karel Everaert
NOPIA research group
Ghent University Hospital
Belgium

Causes

•Acute unilateral edema: deep vein thrombosis, ruptured Baker's cyst, compartment syndrome

•Chronic unilateral edema: venous insufficiency, lymphedema, pelvic tumour, reflex sympathetic dystrophy (CRPS).

•Acute bilateral edema: deep vein thrombosis, sudden deterioration of heart failure or renal disease.

•Chronic bilateral edema: venous insufficiency, heart failure, drugs, idiopathic edema, lymphedema, premenstrual oedema, pregnancy, pre-eclampsia, pulmonary hypertension, obesity, kidney disease (nephrotic syndrome, glomerulonephritis), liver disease, pelvic tumour, continuous sitting with the legs bent (elderly patients who sit for prolonged periods and paralysed patients), anaemia, hypoalbuminaemia, severe hypothyroidism.

History

• Was the onset of leg edema acute or chronic (more than or less than 3 days)? If sudden, be aware of DVT.

• Current medication: It should be checked whether the patient is using medication with the potential of causing edema:
- -calcium-channel blockers and other antihypertensive drugs
- -anti-inflammatory drugs
- -pioglitazone and rosiglitazone (anti-diabetic)
- -corticosteroids
- -sex hormones.

Edema: Diagnosis and Management. KATHRYN P. TRAYES, MD, and JAMES S. STUDDIFORD, MD, SARAH PICKLE, MD, AMBER S. TULLY, MD. American Family Physician, July 15, 2013 Volume 88, Number 2; 102-13

• Systemic diseases (heart, liver and kidney disease)

• Does the patient have a history of pelvic or abdominal cancer or radiotherapy (lymphedema)?

• Does the swelling reduce during the night (reduction occurs in venous insufficiency, but not in lymphedema)?

Physical examination

• Does the patient have pitting edema evidenced by an indent in the skin following finger pressure, most marked over the tibia?
- Pitting = deep vein thrombosis, venous insufficiency, early stages of lymphedema.
- Non-pitting = that remains unchanged overnight is rare = disturbance lymph flow.

• Does the edema cause pain?
- DVT, erysipelas, reflex sympathetic dystrophy (CRPS)» are painful conditions.
- Lymphedema is usually painless.
- Chronic venous insufficiency may cause some aching.

• Any asymmetry of the edema should be determined by measuring the circumference of both calves at their thickest point.

• Skin discoloration may be noted as well as visible varicose veins, in erysipelas, local edema is often present in addition to skin redness and tenderness.

Case

- Female, 77 years old, good general health, no significant daytime LUTS
- Complains about heavy and swollen legs in the evening, no pain since 3 months
- Some dyspnea at excercise
- Complains about nocturia 3x per night

How likely do you consider the following causes of nocturia in this case?

- Overactive bladder
- Sleep disorder
- Idiopathic nocturnal polyuria
- Nocturnal polyuria related to cardiovascular condition

DELPHI PANEL

How appropriate do you consider following diagnostic evaluations?

- Clinical examination focused on cardiovascular pathology
- Bladder diary
- Postvoid residual volume

DELPHI PANEL

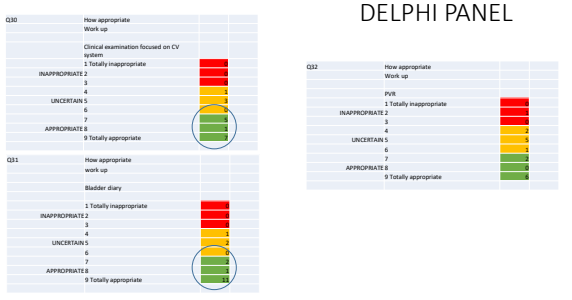
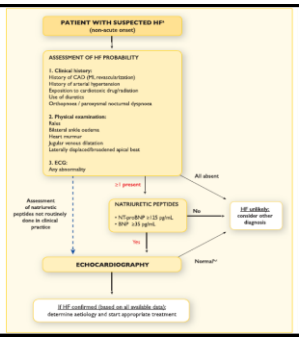


Table 4.1 Symptoms and signs typical of heart failure

Symptoms	Signs
Typical	**More specific**
Breathlessness Orthopnoea Paroxysmal nocturnal dyspnoea Reduced exercise tolerance Fatigue, tiredness, increased time to recover after exercise Ankle swelling	Elevated jugular venous pressure Hepatojugular reflux Third heart sound (gallop rhythm) Laterally displaced apical impulse
Less typical	**Less specific**
Nocturnal cough Wheezing Bloated feeling Loss of appetite Confusion (especially in the elderly) Depression Palpitations Dizziness Syncope Bendopnea[23]	Weight gain (>2 kg/week) Weight loss (in advanced HF) Tissue wasting (cachexia) Cardiac murmur Peripheral oedema (ankle, sacral, scrotal) Pulmonary crepitations Reduced air entry and dullness to percussion at lung bases (pleural effusion) Tachycardia Irregular pulse Tachypnoea Cheyne Stokes respiration Hepatomegaly Ascites Cold extremities Oliguria Narrow pulse pressure

2016 European Guidelines on cardiovascular disease prevention in clinical practice. Eur J Prev Cardiol. 2016 Jul;23(11):NP1-NP96.

For screening:
- **Dyspnea/orthopnea**
- **Fatigue**
- **Ankle swelling**



BNP: the negative predictive values are very similar and high (0.94–0.98) in both the non-acute and acute setting, but the positive predictive values are lower both in the non-acute setting (0.44–0.57) and in the acute setting (0.66–0.67).[1,119–121]

Therefore, the use of BNP is recommended for ruling-out HF, but not to establish the diagnosis.

2016 European Guidelines on cardiovascular disease prevention in clinical practice. Eur J Prev Cardiol. 2016 Jul;23(11):NP1-NP96.

Case – clinical evaluation

- Cardiovascular evaluation: moderate cardiac failure
- Bladder diary: nocturnal polyuria, normal bladder capacity
- No postvoid residual volume

Classifying heart failure

NYHA Class	Patients with Cardiac Disease (Description of HF Related Symptoms)
Class I (Mild)	Patients with cardiac disease but without resulting in limitation of physical activity. Ordinary physical activity does not cause undue fatigue, palpitation (rapid or pounding heart beat), dyspnea (shortness of breath), or anginal pain (chest pain).
Class II (Mild)	Patients with cardiac disease resulting in slight limitation of physical activity. They are comfortable at rest. Ordinary physical activity results in fatigue, palpitation, dyspnea, or anginal pain.
Class III (Moderate)	Patients with cardiac disease resulting in marked limitation of physical activity. They are comfortable at rest. Less than ordinary activity causes fatigue, palpitation, dyspnea, or anginal pain.
Class IV (Severe)	Patients with cardiac disease resulting in the inability to carry on any physical activity without discomfort. Symptoms of heart failure or the anginal syndrome may be present even at rest. If any physical activity is undertaken, discomfort is increased.

The Criteria Committee of the New York Heart Association. *Nomenclature and Criteria for Diagnosis of Diseases of the Heart and Great Vessels*. 9th ed. Boston, Mass: Little, Brown & Co; 1994:253-256.

How appropriate are the following options?

- First treat cardiac failure
- First treat nocturnal polyuria with desmopressin
- First treat nocturnal polyuria with daytime furosemide

DELPHI PANEL

Desmopressin and heart failure

Desmopressin for nocturia is contraindicated in patients with congestive heart failure (New York Heart Association Class II to IV) or uncontrolled hypertension

Desmopressin should be used with caution (e.g., monitoring of volume status) in patients with New York Heart Association Class I congestive heart failure because of the risk of fluid overload and electrolyte abnormalities, patients with heart failure may also be at increased risk for low sodium concentrations.

What if…

- Cardiovascular evaluation: no cardiac failure but uses calcium channel blocker for hypertension
- Bladder diary: nocturnal polyuria, normal bladder capacity
- No postvoid residual volume

Strength of Recommendations

Key clinical recommendation	*Label*	*References*
Treatment with an angiotensin-converting enzyme inhibitor or angiotensin-receptor blocker should be considered in patients with calcium channel blocker–induced pedal edema.	A	29, 30
Spironolactone (Aldactone) should be used to decrease morbidity and mortality rates in patients with NYHA class III or IV heart failure.	B	15
The use of a transjugular intrahepatic portosystemic shunt may be superior to large-volume paracentesis in relieving ascites and prolonging survival.	B	22, 23
Travel stockings (i.e., "support hose") should be worn during flights longer than seven hours to prevent edema and DVT.	B	27
Spironolactone should be used in patients with cirrhosis and grade 2 or 3 ascites to combat hyperaldosteronism.	C	18
Paracentesis is the treatment of choice in patients with grade 3 ascites and should be used in conjunction with sodium restriction and diuretic therapy.	C	18
Long-term use of compression garments in conjunction with meticulous skin care and avoidance of blood pressure measurements and other constrictions should be considered in patients with lymphedema.	C	34

NYHA = New York Heart Association; DVT = deep venous thrombosis.

A = consistent, good-quality patient-oriented evidence; B = inconsistent or limited-quality patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, opinion, or case series. See page 2029 for more information.

Treatment of Edema. JAMES G. O'BRIEN, M.D., and SHOBHA A. CHENNUBHOTLA, M.D., RAMANA V. CHENNUBHOTLA, M.D. American Family Physician, June 1, 2005 Volume 71, Number 11, 2111-7

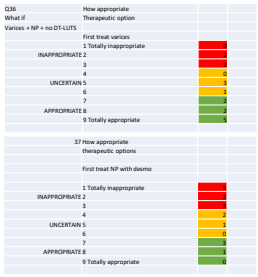
What if…

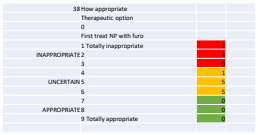
- Cardiovascular evaluation: no cardiac failure but varicose veins at lower limbs
- Bladder diary: nocturnal polyuria, normal bladder capacity
- No postvoid residual volume

What if? No cardiac pathology, but varicose veins

- First treat varicose veins
- First treat nocturnal polyuria with desmopressin
- First treat nocturnal polyuria with daytime furosemide

DELPHI PANEL





EBM

Table 6. Strength of Evidence for Major Recommendations

	Strength of Recommendation*
Diagnostic recommendations	
Relative frequencies of causes of edema in Tables 1–3[1,4,53]	C
Clinical findings that help distinguish venous edema, lymphedema, and lipidema[8,9,11,12,21,22,24]	C
Important components of the patient history[8–12,21,24]	C
Important components of physical exam[9,10–12,22,24]	C
Echocardiogram recommended in patients over age 45[4]	C
Medications that cause edema[4,13,14,16,17,24,55]	C
Normal D-dimer rules out deep vein thrombosis[25,56]	B
Use of Doppler exam to confirm or rule out deep vein thrombosis[35–39]	B
Treatment recommendations	
Diuretics to treat venous insufficiency[2]	C
Horse chestnut seed extract to treat venous insufficiency[41–44]	B
Compression stockings to treat venous insufficiency[40]	C
Diuretics to treat idiopathic edema[5,31,46]	C

* Strength of recommendation classified according to the 3-component SORT system[45]: A, denotes recommendation based on consistent and good-quality patient-oriented evidence[45]; B, denotes recommendation based on inconsistent or limited-quality patient-oriented evidence[45]; C, denotes recommendation based on consensus, usual practice, opinion, disease-oriented evidence, or case series for studies of diagnosis, treatment, prevention, or screening.[45]

Approach to Leg Edema of Unclear Etiology
John W. Ely JABFM March–April 2006 Vol. 19 No. 2

Summary

- Oedema and specially leg oedema causes nocturnal polyuria and nocturia through resorption of the fluid when supine resulting in an immediate excess in urine output and a delayed increase in ANP related salt diuresis
- Leg oedema are seen with liver, heart or kidney disease or following varices of the legs, lack of physical activity or muscle paralysis
- Medications can cause leg edema
- Diagnosis/therapy are based on expert opinion rather than science and the available guideline documents do not mention nocturia.
- Normal BNP excludes heart failure
- Desmopressin is contraindicated from class 2 HF or higher and careful monitoring needed if class 1

Blood Pressure and nocturnal LUTS

Dr Michael Whishaw, FRACP
RMH Continence & Urology Services

ICS Philadelphia 28 August, 2018

The Royal Melbourne Hospital

Michael Whishaw

Affiliations to disclose†:

Ferring Pharmaceuticals Australia – consultant
Astellas - speaker

† All financial ties (over the last year) that you may have with any business organisation with respect to the subjects mentioned during your presentation

Funding for speaker to attend:

- [X] Self-funded
- [ ] Institution (non-industry) funded
- [ ] Sponsored by:

Nocturia

Many papers

- Associated with many systemic disease
  - (Poorly controlled) diabetes and metabolic syndrome
  - Hypertension and congestive heart failure
  - Autonomic dysfunction
  - Impaired circulation
  - Renal
  - Malignant disease
  - Sleep disordered breathing
  - Anxiety

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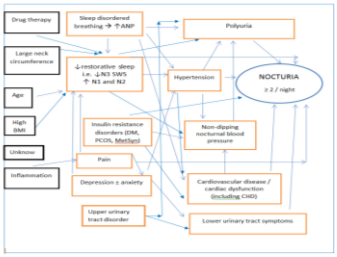
Nocturia – causal inter-relationships: outcome of a literature review Bower 2017



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Targeting Aetiology of Nocturia Guides Outcomes

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Targeting Aetiology of Nocturia Guides Outcomes

⇣

TANGO Nocturia Tool

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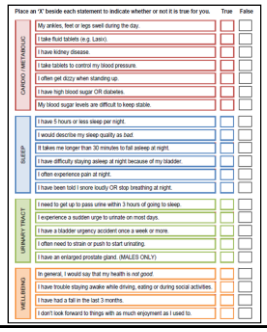

TANGO Nocturia Screening Tool

Bower WF et al. TANGO - a screening tool to identify comorbidities on the causal pathway of Nocturia. BJU Int. 2017;119(6):933-41.

Rose GE et al. Reliability testing of the TANGO Short-Form nocturia screening tool. ANZCJ. 2017; 23(3):68-74.

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Targeting Aetiology of Nocturia Guides Outcomes

- 22 item questionnaire
- Patient-completed
- Fully validated
- Red flags for all-cause nocturia

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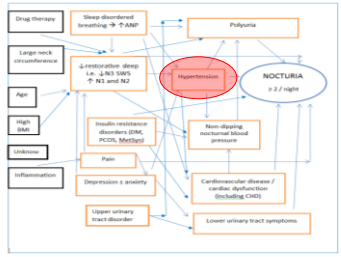
Nocturia – causal inter-relationships outcome of a literature review Bower 2017



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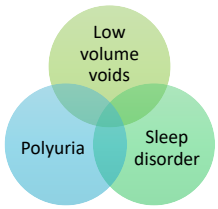
Nocturia - pathophysiology



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Nocturia - pathophysiology

- Small volume voids
  - Detrusor overactivity
  - Impaired emptying
- Nocturnal polyuria
- Combination of these – common
- 1° sleep disturbance

- Defined on a bladder diary

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Bladder diary

72yo M: No surgery; PVR 20 ml
OAB – detrusor overactivity
NPi = 1335mL/1960mL = 68%

Time	Type drink	Amount drink	Time	Amount urine passed	Degree of Leakage				Comments
					Dry	Damp	Wet	Soaked	
			0100	275 ml			X		Woke wet
			0310	290 ml	X				Urinal
			0820	260 ml	X				Urinal
			0545	270 ml		X			Woke wet
			0650	240 ml		X			At toilet
0730	Milk	300 ml							
0815	Coffee	250 ml							
			0900	130 ml		X			At toilet
1100	Water	300 ml							
			1145	125 ml	X				
1320	Tea	500 ml							
			1420	170 ml	X				
1500	Tea	250 ml							
			1810	110 ml		X			At toilet
1915	Wine	300 ml							
2230	Water	150 ml							
			2235	90 ml	X				
Total		2050 ml	Total	1960 ml					

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Hypertension and nocturia

- Clear association
  - In 11 of 15 identified papers — Feldstein 2013
  - OR 1.30-2.68 with nocturia>1 — Yoshimura 2004
  - Likely contribution from coexistent comorbidity
- As independent variable
  - Absence of comorbidity — Yoshimura 2004; Johnson 2005; Parthasarathy 2012; Victor 2017
  - No evidence nocturia predicts hypertension — Lightner 2012

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Hypertension and nocturia

- Mechanisms
  - Mainly promoting nocturnal polyuria
  - Effects on glomerular filtration and tubular transport causing natriuresis (renin-angiotensin and prostaglandin systems) Romero 1988
  - Glomerular hyperfiltration — Brenner 1996; Palatini 2012
  - 2° - related to hypertensive comorbidities

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Circadian rhythm and BP

- Normal ↓ in nocturnal BP by at >=10 mm Hg
  - Mainly due to ↓heart rate – physical activity, autonomic function, sodium sensitivity — Agarwal 2010
- Its absence = "non-dipping hypertension"
  - Occurs in 25% of hypertensives
  - Mechanism multifactorial
- Non-dipping hypertension
  - Definite association with nocturia — Perk 2001; Obayashi 2015
  - Possible mechanisms
    - ↑renal perfusion
    - ↑ in nocturnal physical activity — Agarwal 2010

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Non-dipping hypertension

- Equates to nocturnal hypertension
- Associations — Agarwal 2010
  - Chronic kidney disease
  - OSA
  - Heart failure
  - Metabolic syndrome
- Implications — Pickering 2001
  - Renal disease progression
  - Greater end-organ damage
  - ↑cardiovascular mortality

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Hypertension and SDB

- Obstructive sleep apnoea (OSA) associations
  - obesity
  - ↑ SNS activity
  - hypertension — Narkiewicz 1997
  - nocturia — Niimi 2016
- Nocturia predicts hypertension in OSA — Sugaya 2001, Destors 2014,5
- Early morning hypertension predicts OSA — Hongyo 2016
- Rx for OSA is usually CPAP
  - ↓ in nocturia is then common

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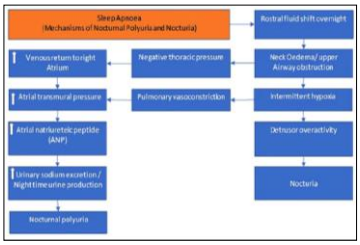
OSA and nocturia – proposed mechanisms

Kass-Iliyya, Hashim 2018



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Orthostatic (postural) hypotension

- Feature of autonomic dysfunction
- Parkinson's Disease a common cause
- Nocturnal polyuria very common
  - ↓renal perfusion when upright
  - ↑renal perfusion when supine

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90yo Male

- Past History
  - Rheumatoid arthritis 1998
  - TURP 2004
  - Low-grade lymphoproliferative disorder – no Rx
  - Severe postural hypotension
  - Subsequent Dx of Parkinson's Disease, and (later) dementia
- Medications
  - Salazopyrine, sertraline.
  - Later levodopa
- LUTS
  - Daytime 6 - 10
  - Nocturia 4 - 8
  - Urgency usual
  - Urgency leakage >=once a day
  - Voiding "normal"

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Examination

- Blood pressure
  Supine 180/95mmHg
  Standing 120/80mmHg
- No ankle oedema
- Void 135 mL
  PFR 8 mL/s
  PVR 25 mL
- Poor balance

Investigations

- Bladder diary
  - Voids 50-150mL daytime, up to 300mL nocte
  - Overnight output 780mL NPi 61%
  - FUST as low as 1 hour
- Urinary tract US
  - Prostate volume 93ml
- Urodynamics
  - Detrusor overactivity
  - No obstruction

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Formulation

- Nocturia
  - Detrusor overactivity
  - Nocturnal polyuria (due to postural hypotension)
- Poor balance
- (Dementia)
- Wife assisting with toileting

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Management

- Detrusor overactivity
  - Caffeine limitation
  - Oxybutynin
  - Changed later to mirabegron because of cognitive decline
  - (Limit nocte fluid intake)
- Postural hypotension
  - Fludrocortisone
  - Midodrine
  - Below-knee compression
- Overall limited success re nocturia

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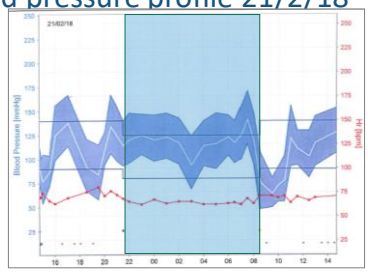
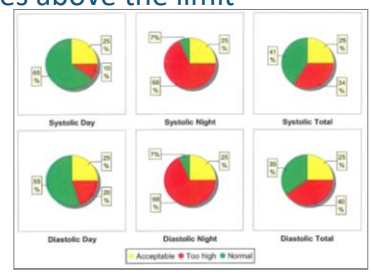
Blood pressure profile 21/2/18



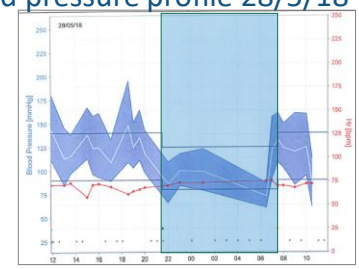
Values above the limit



Management

- Formulation
  - Nocturnal hypertension
- Treatment
  - Glyceryl trinitrate 25-50 mg transdermal patch
    - Overnight while in bed
- Outcome
  - ↓Nocturia
    - February 4-7 voids, average 5
    - May 0-6 voids, average 2

Blood pressure profile 28/5/18



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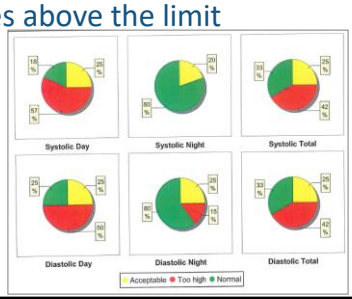
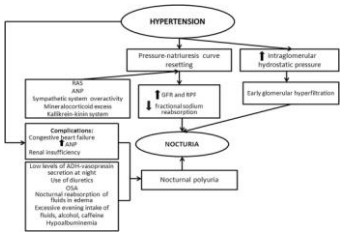


Hypotensives and nocturia

- Many studies show correlation — Bulpitt 1999
- Drug groups
  - diuretics — Asplund 2002; Kupelian 2009
    - thiazides – long half life
    - loop diuretics – timing may be relevant
      - furosemide 6hrs before bed ↓nocturia — Reynard 1998
  - calcium channel blockers — Hall 2012
    - fluid-retaining (especially amlodipine)

Hypertension and nocturia - Proposed mechanisms

Feldstein 2013



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Summary

- Are we meeting the needs of older people with nLUTS?
  - Nocturia is a marker for poor health
  - Blood pressure clearly associated with nocturia
  - Consider nocturnal hypertension in persisting nocturia
  - Review hypertension Rx regimen in persisting nocturia

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References

Available on request:

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Hypertension and nocturia are linked by -

- Common causal pathways
- Peripheral oedema
- Increased glomerular filtration
- Pharmacotherapy effects

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Postural hypotension should be actively identified in patients with nocturia because -

- Balance is related to nocturia
- It is often not clinically obvious
- It is a nocturnal phenomenon
- It is caused by hypovolemia

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It is important to evaluate sleep quality in someone with nocturnal LUTS because -

- Sleep disruption means people toilet when their bladder is not full
- Sleep disruption can increase diuresis
- Needing to void early in the night is an important diagnostic marker
- There may be an environmental issue disrupting sleep

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