Dementia

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Neuro-Urology

The management of neurogenic lower urinary tract dysfunction in spinal cord injured patients was the core competence of neuro-urology and the spinal cord injury was the human model for treatment.

However, neuro-urology in times of an aging population must take into account a sharp increase of bladder dysfunctions due to cerebral lesions.

The need for neuro-urolological management in these patients is therefore increasing.
# LUTS in cortical and subcortical lesions

**Appearance, prevalence, symptoms**

<table>
<thead>
<tr>
<th>Disease</th>
<th>Onset</th>
<th>Prevalence</th>
<th>Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>M. Parkinson</td>
<td>Late</td>
<td>ca. 70%</td>
<td>OAB, especially nocturia, urgency incontinence</td>
</tr>
<tr>
<td><em>(ca. 18.000 in Austria)</em> (8,1 mio inhabitants)</td>
<td></td>
<td></td>
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<tr>
<td>Multi-System Atrophy</td>
<td>Early (maybe first symptom at all)</td>
<td>100%</td>
<td>Incontinence (detrusor and sphincter related) PVR</td>
</tr>
<tr>
<td>Alzheimer’s Dementia</td>
<td>Late</td>
<td>80-100%</td>
<td>Unawareness Urinary Incontinence</td>
</tr>
<tr>
<td><em>(ca. 160.000 in Austria)</em> <em>(Increase 20.000/year)</em></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Levy Body Dementia</td>
<td>Early</td>
<td>100%</td>
<td>OAB</td>
</tr>
<tr>
<td>Stroke</td>
<td>after one year</td>
<td>20%</td>
<td>OAB, incl. urgency urinary incontinence</td>
</tr>
<tr>
<td><em>(Incidence 20.000/year)</em> <em>(Prevalence 60.000 in Austria)</em></td>
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<td></td>
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</tbody>
</table>
NEURODEGENERATION
is the umbrella term for the progressive loss of structure or function of neurons, including death of neurons. Many neurodegenerative cerebral diseases including Parkinson’s, Alzheimer’s, and Huntington’s occur as a result of neurodegenerative processes. As research progresses, many similarities appear that relate these diseases to one another on a sub-cellular level.
Neurodegeneration can be found in many different levels of neuronal circuitry ranging from molecular to systemic and may therefore also cause lower urinary tract symptoms.
Definition of Dementia

ICD-10 Definition (F01x – F03x):
„Aquired disturbance of memory and formal thinking in a way, that the all-day-life is impaired. The symptoms have to be aware at least 6 months. Temporary impairments of cognitiv functions, like delirium, do not count as dementia.“

However:
Symptomatology of dementia is more complex as simple „loss of memory“
– Inability of reception, storage, process and reproduction of informations
– Loss of familiar, memorized procedures
– Loss of the ability for multitask activities
– Loss of the capability to judge and deduct
Dementias & LUTS
Topics

• Data acquisition & Flow diagram (according to the PRISMA statement)
• Types of Dementia
• Why is important for the urologist to know the different types of dementia?
• Causes of LUTS in demented patients
• Conclusions and Recommendations
DATA ACQUISITION

The Pubmed/Embase research terms (Oct 2013)

1. Dementia
2. Vascular dementia
3. Alzheimer's disease
4. Dementia Alzheimer's disease
5. Dementia with Lewy bodies (DLB)
6. Frontotemporal dementia
7. Creutzfeldt-Jacob disease
8. Normal pressure hydrocephalus
9. Huntington`s disease
10. Wernicke-Korsakoff syndrome

Each of these terms was crossed with:

1. Bladder dysfunction
2. Sphincter dysfunction
3. Urinary incontinence
4. Urinary symptoms
5. Urinary retention
6. Urinary infection
7. Bladder catheter
8. Urological care
Records identified through database searching (n = 1913)
Additional records identified through other sources (n = 20)
Records after duplicates removed (n = 519)
Records screened (n = 1414)
Records excluded (n = 1352)
Full-text articles assessed for eligibility (n = 62)
Full-text articles excluded, with reasons (n = 26)
Studies included in quantitative synthesis (n = 36)
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## Classification of Dementia
### Etiology

<table>
<thead>
<tr>
<th>Neuro-degenerative etiology</th>
<th>Other forms</th>
</tr>
</thead>
<tbody>
<tr>
<td>M. Alzheimer (AD)</td>
<td>Vascular 20%</td>
</tr>
<tr>
<td>50%</td>
<td>Normal-Pressure-Hydrocephalus (NPH)</td>
</tr>
<tr>
<td>Lewy-Body-Disease (LBD)</td>
<td>Neoplasia, Traumata</td>
</tr>
<tr>
<td>15%</td>
<td>Chronic intoxikations</td>
</tr>
<tr>
<td>Cortico-basal degeneration</td>
<td>Infections of the CNS (Lues, AIDS)</td>
</tr>
<tr>
<td>Progressive-focal degeneration</td>
<td>Non-infection-associated inflammations</td>
</tr>
<tr>
<td></td>
<td>Pseudodementia in psychiatr. diseases</td>
</tr>
<tr>
<td></td>
<td>Other structural defects:</td>
</tr>
<tr>
<td></td>
<td>cerebral hypoxia</td>
</tr>
<tr>
<td></td>
<td>radiatio</td>
</tr>
</tbody>
</table>
Types of dementia

**Alzheimer’s Dementia**
- Alzheimer's disease (AD) is the most common form of dementia (60%)

**Vascular Dementia**
- It is the second most common form of dementia (20%)

**Dementia with Lewy Bodies (DLB)**
- It is the third most common form of dementia (10%)

**Normal Pressure Hydrocephalus (NPH)**
- Prevalence 3%

Types of dementia

Alzheimer’s Dementia

- Alzheimer's disease (AD) is the most common form of dementia (60%)
  - Early symptom = short memory loss
  - Later = long-term memory loss, confusion, irritability, aggression, mood swings, trouble with language
  - No cure

Vascular Dementia

- It is the second most common form of dementia (10%)

Dementia with Lewy Bodies (DLB)

- It is the third most common form of dementia (3.5 per 100,000 person-years)

Normal Pressure Hydrocephalus (NPH)

- Prevalence 3%

Types of dementia

Alzheimer’s Dementia
• Alzheimer's disease (AD) is the most common form of dementia (60%)

Vascular Dementia
• It is the second most common form of dementia (10%)
  • Caused by problems in the blood supply to the brain, typically by a series of minor strokes.
  • Cognitive impairment after one or many cerebrovascular events.
  • Early detection and accurate diagnosis are important, as vascular dementia is at least partially preventable.

Types of dementia

- Alzheimer's Dementia (AD)
  - Alzheimer's disease (AD) is the most common form of dementia (60%)

- Vascular Dementia
  - It is the second most common form of dementia (10%)

- Dementia with Lewy Bodies (DLB)
  - It is the third most common form of dementia (3.5 per 100,000 person-years)

- Normal Pressure Hydrocephalus (NPH)
  - Prevalence 3%

Lewy bodies are abnormal proteins deposits within neurons (clumps of alpha-synuclein and ubiquitin proteins, which are detectable in post mortem brain histology).

Cortical dementia with fluctuation, in some cases psychosis

Rapid onset and progression

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Types of dementia

- Alzheimer's Dementia
  - Alzheimer's disease (AD) is the most common form of dementia (60%).

- Vascular Dementia
  - It is the second most common form of dementia (10%).

- Dementia with Lewy Bodies (DLB)
  - It is the third most common form of dementia (3.5 per 100,000 person-years).

- Normal Pressure Hydrocephalus (NPH)
  - Prevalence 3%
    - Caused by decreased absorption of cerebrospinal fluid.
    - Typical symptoms: gait disturbance, urinary incontinence, and dementia.
    - This is the only type of dementia that is potentially reversible (shunt surgery).

Normal pressure hydrocephalus (NPH)

*Symptom TRIAS according literature:*

1. **Astasia/Abasia**

2. **Dementia**
   - 3% of all dementias
   - primary reversible dementia (shunt operation)

3. **Urinary incontinence**
   - only in 43% of NPH patients;
   - is not a symptom indicating the beginning of dementia
   - is an autonomic symptom causing neurogenic lower urinary tract dysfunction
Dementias & LUTS
Topics

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• Why is it important for the urologist to know the different types of dementia?
• Causes of LUTS in demented patients
• Conclusions and Recommendations
Why is it important for the urologist to know the different types of dementia?

1. Because the occurrence of LUTS during the course of the disease is different
2. The type of LUTS and, therefore, the urological management are distinct too

Savica R, Grossardt BR, Bower JH, Boeve BF, Ahlskog J, Rocca WA. Incidence of Dementia With Lewy Bodies and Parkinson Disease Dementia. JAMA Neurol. 2013
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CAUSES OF LUTS IN DEMENTED PATIENTS

1. Neurological disease itself
2. Neurological pharmacotherapy
3. Comorbidities
Alzheimer’s Disease

- In Alzheimer’s disease (ALD), the prevalence of IU, usually unawareness urinary incontinence, ranges from 23% to 48% and the onset of incontinence usually occurs in late-stage dementia. (LE 3)
- Behavioural therapy strategies, including toilet training and prompted voiding, are especially useful and should be started earlier enough to induce reflex behaviour, which can be used later, when dementia progresses (going to the toilet = micturition/defecation; glass of water = drinking). (LE 5/GR C*)
- Antimuscarics may enhance behaviour therapy, especially when the bladder capacity is reduced. (LE 5/GR C*)
Passive Training Programs – contraindications

• **Is ineffective and should not be used** in persons who are unable to state their name or need the assistance of more than one person to transfer, these persons should be managed with “check and change” (Level 1)

• **Should not be continued** in eligible persons who, after a three day trial, have less than a 20% reduction in wet checks (Level 1) or toilet successfully less than two-thirds of the time; these persons should be managed with “check and change” (Level 1)
Type of dementia and LUTS

Lewy Bodies Dementia

• In contrast to Alzheimer’s dementia, LUTS usually occur earlier during the course of the disease or can even precede severe mental failure in Lewy Bodies Dementia (LBD). (LE 3)

• Symptoms of overactive bladder (OAB) and detrusor overactivity are more common in LBD (and in vascular dementia), than in patients with ALD. (LE 3)

• The symptoms and urodynamics are useful for differential diagnosis, and are therefore helpful for the neurologist (LE 3/GR C*)

Lewy-Body-Disease (LBD)

Differential Diagnosis:
M. Alzheimer, M. Parkinson or atypical forms of Parkinson for the neurologist sometimes difficult

Urodynamics may help in differential diagnosis
OBJECTIVE:
The present study sought to investigate lower urinary tract symptoms and urodynamic and cystometric findings in Parkinson disease (PD), dementia with Lewy bodies (DLB), and Alzheimer disease (AD).

CONCLUSIONS:
Urgency and urge incontinence suggest detrusor overactivity, which was more prevalent in dementia with Lewy bodies than in Parkinson disease and Alzheimer disease, whereas mean voided volume, free flow, cystometric bladder capacity, and detrusor pressor were similar in the groups. Frequency of micturition could not be reliably assessed in patients with dementia.
## Micturition charts

<table>
<thead>
<tr>
<th></th>
<th>n</th>
<th>MF (24h)</th>
<th>mean micturition volume</th>
<th>urgency episodes n/24h</th>
<th>Incontinence-episodes (n/24h)</th>
</tr>
</thead>
<tbody>
<tr>
<td>LBD</td>
<td>15</td>
<td>7,9 ± 3,4</td>
<td>198 ± 79</td>
<td>14,1</td>
<td>8,2</td>
</tr>
<tr>
<td>PD</td>
<td>15</td>
<td>6,4 ± 1,5</td>
<td>196 ± 53</td>
<td>7,7</td>
<td>3,8</td>
</tr>
<tr>
<td>AD</td>
<td>16</td>
<td>5,9 ± 1,6</td>
<td>165 ± 71</td>
<td>3,3</td>
<td>2,3</td>
</tr>
<tr>
<td>p</td>
<td></td>
<td>0,34</td>
<td>0,48</td>
<td>&lt;0,001</td>
<td>0,04</td>
</tr>
</tbody>
</table>

KW ANOVA (p), x2 (p)
## Urodymanics

<table>
<thead>
<tr>
<th></th>
<th>n</th>
<th>Cystomert. cap. (ml)</th>
<th>Max. detrusor pressure</th>
<th>Detrusor-hyperactivity</th>
<th>DSD</th>
</tr>
</thead>
<tbody>
<tr>
<td>LBD</td>
<td>12</td>
<td>254 ± 185</td>
<td>38,5 ± 33,7</td>
<td>11 (92%)</td>
<td>-</td>
</tr>
<tr>
<td>PD</td>
<td>13</td>
<td>256 ± 76</td>
<td>42,2 ± 19,4</td>
<td>6 (46%)</td>
<td>-</td>
</tr>
<tr>
<td>AD</td>
<td>10</td>
<td>297 ± 154</td>
<td>45,8 ± 21,5</td>
<td>4 (40%)</td>
<td>-</td>
</tr>
<tr>
<td>p</td>
<td></td>
<td>0,97</td>
<td>0,21</td>
<td>0,02</td>
<td></td>
</tr>
</tbody>
</table>

*KW ANOVA (p), x2 (p)*

Ransmayr et al. 2008
Type of dementia and LUTS

NPH

- LUTS have been reported in up to 93% of the patients with idiopathic Normal Pressure Hydrocephalus (NPH), in which the most frequent symptoms were urgency (64%), frequency (64%) and UI (57%).
- NPH (as well as vascular dementia) manifests with gait disturbance, dementia and UI.
- Symptoms of NPH may be reversed by shunt surgery (such as ventriculo-peritoneostomy). However, UI and dementia are twofold less likely to improve than gait disturbance. *(LE 2)*

CAUSES OF LUTS IN DEMENTIA PATIENTS

1. Neurological disease itself
2. Neurological pharmacotherapy
3. Comorbidities
Symptomatic therapy

Drug treatment: Neurotransmitter
• Cholinesterase inhibitors (AChE-I)
  - Donepezil
  - Galantamin
  - Rivastigmin
• Memantine

Non-drug based treatments
• Psychomotoric reeducation
• Psychologic interventions
• Memory training
PHARMACOTHERAPY FOR DEMENTIA

- First-line treatment: cholinesterase-inhibitors
- Second-line treatment: memantine

Cholinesterase-Inhibitors* and memantine are given by the neurologist to increase acetylcholine activity in the brain by stimulation M1 receptors.

But Cholinesterase-Inhibitors may also be effective in the periphery, thus inducing/increasing urge-incontinence. *Deterioration of continence may be misinterpreted as disease progression and antimuscarinics are therefore given to this patients.*

*Donepezil - Arizept®, Rivastigmine - Exelon®, Galantamine - Reminyl®
* Memantine - Namenda®
Likelihood of urinary incontinence in Alzheimer patients

Simple review of 3 papers

“Cholinesterase inhibitor treatment was associated with significant worsening of urinary continence.”

“There was no significant difference between Rivastigmine and Donepezil”

“… approximately 7% risk of precipitating urinary incontinence and current incontinence may be significantly worsened.”

The Dilemma with Antimuscarinics in OAB Patients treated with Cholinesterase-Inhibitors for Cognitive Impairment

- Cholinesterase-inhibitors are given by the neurologist to improve memory
- Antimuscarinics are given by the urologist to improve urgency

Antimuscarinics crossing the blood-brain barrier (BBB) and/or are bound to the M1 receptors, block them for acetylcholine.

Thus, rapid (2-3 days) deterioration of cognition (delirium, hallucinations) can occur.

Safe antimuscarinics: Propiverine, Trospium, Darifenacine, (Solifenacine)
OAB and memory disorders increase

Decline in delayed memory recall relative to age 20–29 (%)\(^1\)

OAB prevalence (%)\(^2\)

\(^2\)Milsom I, et al. BJU Int 2001;87:760–6
CAUSES OF LUTS IN DEMENTIA PATIENTS

1. Neurological disease itself
2. Neurological pharmacotherapy
3. Comorbidities
• LUT problems in patients with dementia are not necessarily related to the neurologic pathology

• Other diseases such as prostate pathology and pelvic organ prolapse might also have an influence

• Clinical assessment including history, clinical examination, urine analysis, bladder diary, free flowmetry and PVR should be as comprehensive as possible (LE 5/GR A*)
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Conclusions

• Overall, urinary incontinence (UI) affects around 50% of men and 60% of women with dementia, occurring in advanced stages of disease. (LE 3)

• Onset, characteristics and etiology of LUTS vary according to the type of dementia, effects of neurological pharmacotherapy and comorbidities. (LE 3)
RECOMMENDATIONS

1. Despite of the type of dementia, the treatment of LUTS should be tailored to individual patient needs and disease status, taking into account factors like mobility, cognitive function and general medical condition. (LE 3/4, GR C)

2. Conservative management includes prompted voiding, toilet training and oral antimuscarinics. (LE 3/4, GR C)

3. Aggressive therapy of incontinence must be reserved for patients with good general status and ambulation. (LE 5, GR C*)
RECOMMENDATIONS

4. Clinicians should consider the possible contributing role of cholinesterase inhibitors in new-onset or worsening urinary incontinence and the potential risk of coprescribing cholinesterase inhibitors + antimuscarinics to patients with dementia. (LE 4, GR B*)

5. Be careful in treating OAB with antimuscarinics (consider CNS side effects) and detect cognitive changes (LE 3/4, GR B*), safe antimuscarinics in this regard are Propiverine, Trospium, Darifenacine (Solifenacin) – avoid oral Oxybutynin (EAU Guidelines 2014).