Bahan Ajar 3

Neurogenic Bladder

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2016

Pendahuluan

- *Neurogenic Bladder* (NB) atau dikenal dgn istilah *neurogenic lower urinary tract dysfunction* (NLUTD) → disfungsi vesika urinaria dan uretra terkait dgn penyakit pd SSP atau saraf perifer.

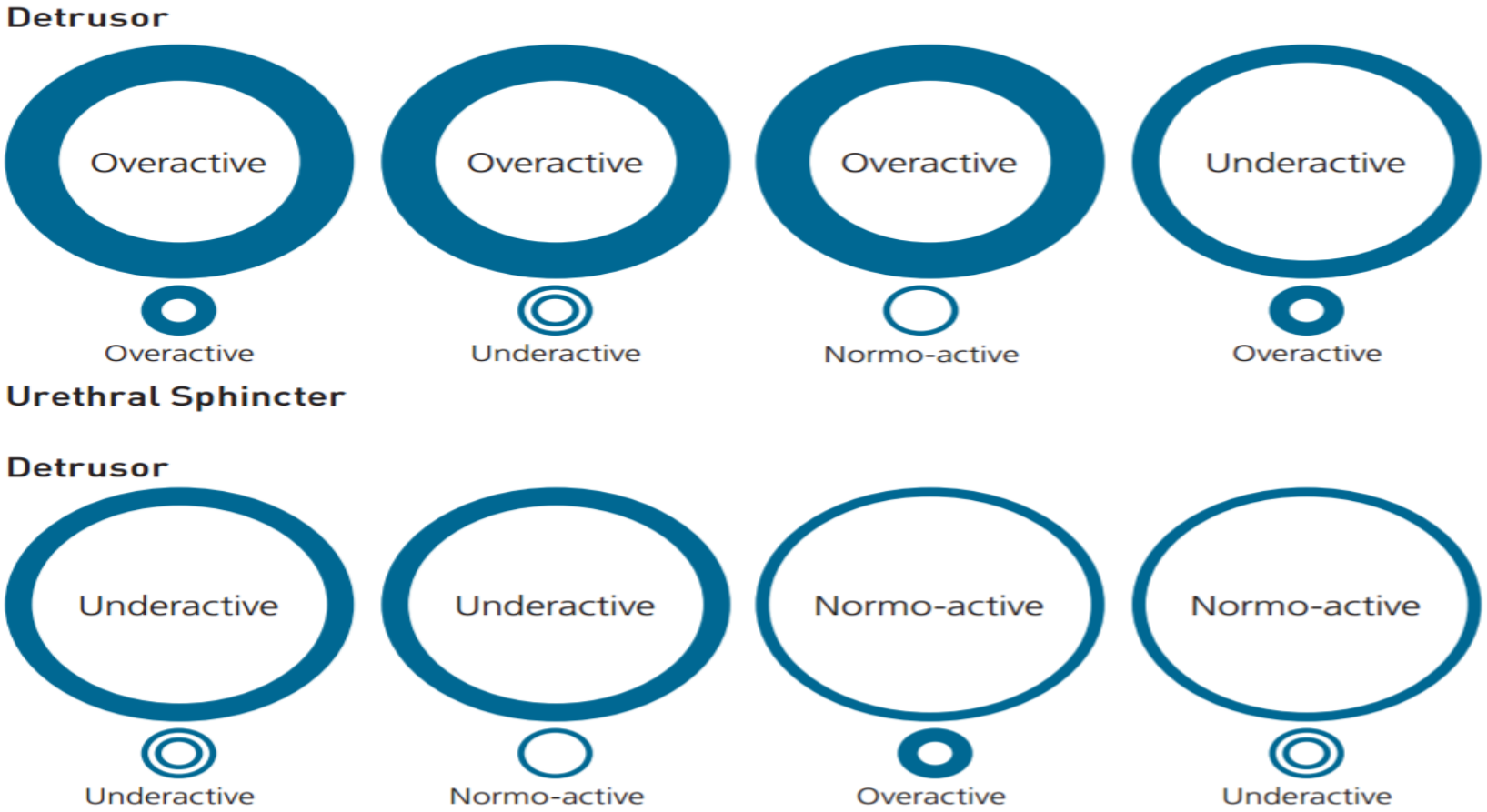
Table 1. Liao's comprehensive classification system for lower and upper urinary tract dysfunction (LUUTD) in patients with neurogenic bladder.

Lower Urinary Tract		Upper Urinary Tract
Storage	**Voiding**	
1. Bladder function	**1. Bladder function**	**1. Vesico-ureteral reflux**
(1) Detrusor activity	(1) Detrusor contractility	(1) No
① Normal	① Normal	(2) Yes: Unilateral, bilateral
② Overactive	② Underactive	Degree (left, right)
	③ Acontractile	I
2. Bladder sensation		II
(1) Normal	**2. Urethral function**	III
(2) Increased or hypersensitive	(1) Normal	IV
(3) Reduced or hyposensitive	(2) Obstruction	V
(4) Absent	① Urethral overactivity	
	• Detrusor external sphincter dyssynergia	**2. Upper urinary tract dilatation: hydronephrosis and ureteral dilatation**
3. Bladder capacity	• Detrusor bladder neck dyssynergia	(1) No
(1) Normal (300–500 mL)	• Sphincter overactivity	(2) Yes: Unilateral, bilateral
(2) High (>500 mL)	• Non-relaxing sphincter	Grade (left, right)
(3) Low (<300 mL)	• Non-relaxing bladder neck	1
	② Mechanical obstruction	2
4. Bladder compliance		3
(1) Normal (20–40 mL/cmH_2O)		4
(2) High (>40 mL/cmH_2O)		
(3) Low (<20 mL/cmH_2O)		**3. Ureteral obstruction in bladder wall**
		(1) No
5. Urethral function		(2) Obstruction (left, right)
(1) Normal		
(2) Sphincter acontractility		**4. Renal function**
		(1) Normal
(3) Incompetent		① Unilateral kidney: GRF ≥ 70 mL/min (left, right)
		② Both kidneys: Total GRF ≥ 70 mL/min
① Bladder neck		(2) Renal insufficiency (Total GRF: 50–70 mL/min)
		① Compensatory (Total GRF ≥ 50 mL/min, Scr < 178 μmol/L)
② External sphincter		② Decompensation (Total GRF < 50 mL/min, Scr ≥ 178 μmol/L)

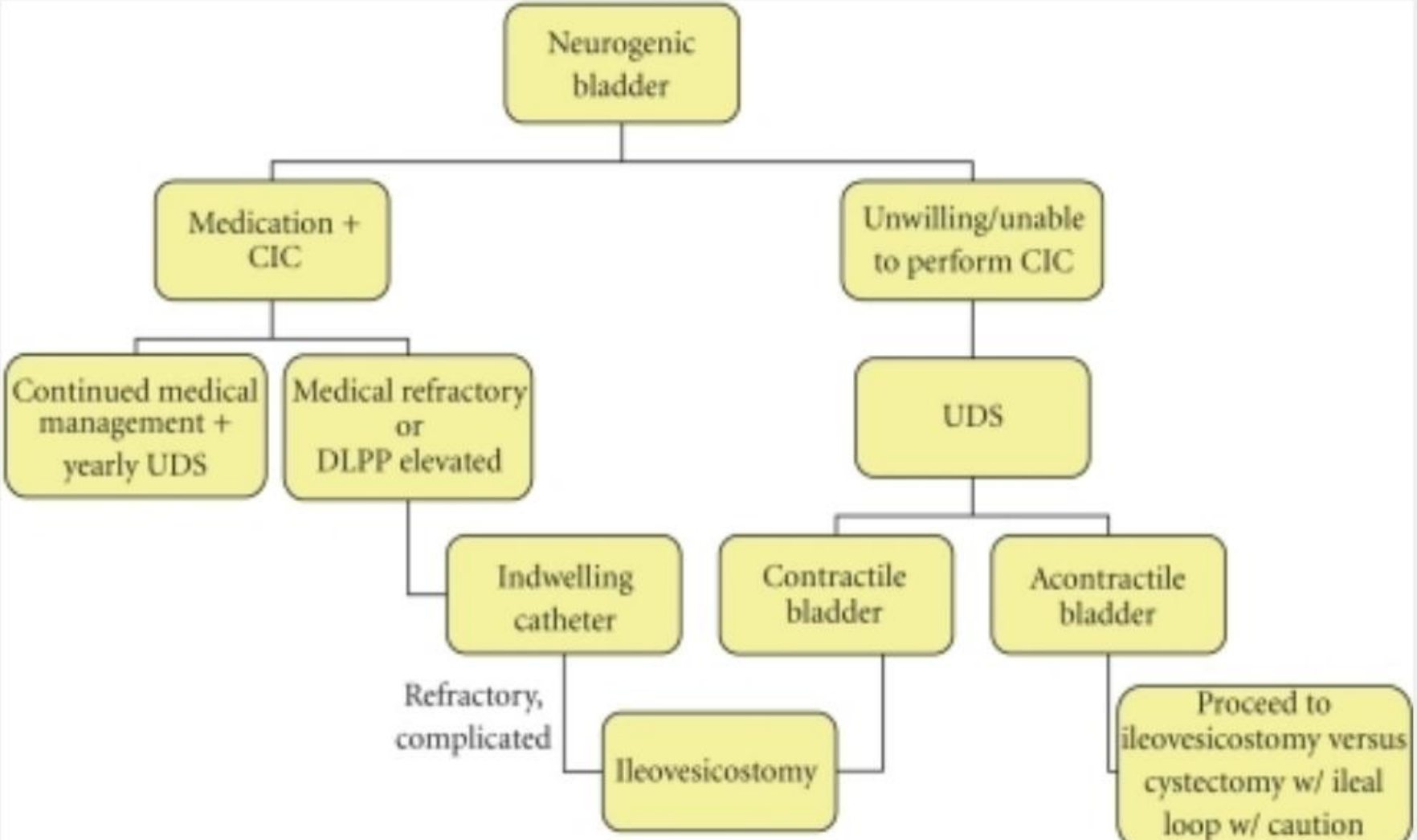
TABLE 1 – Types of Neurogenic Bladder Impairment

Suprasacral (Infrapontine) Bladder
An upper motor neurone lesion (releasing automatic sacral reflex micturition centre from descending inhibition) results in: • detrusor hyperreflexia (overactivity). • detrusor-external sphincter dyssynergia (DESD), referring to inappropriate co-contraction of the external urethral sphincter (EUS) with voiding detrusor contraction.
Mixed Neurogenic Bladder (Type A)
A lesion in the conus medullaris with damage to detrusor (parasympathetic) nucleus causes: • detrusor hyporeflexia (underactivity) with external sphincter hyperreflexia. • characteristically large volume with overflow incontinence.
Mixed Neurogenic Bladder (Type B)
A lesion in the conus medullaris involving pudendal (somatic) nucleus causes: • detrusor hyperreflexia with external sphincter hypotonia. • small volume, high frequency, incontinence.
Infrasacral Bladder
A Lower Motor Neurone lesion from conus medullaris and/or cauda equina damage results in: • areflexia (not atonia) of detrusor (due to post-ganglionic fibres being in bladder wall) and areflexia with atonia of pelvic floor muscles. • may have isolated increase in bladder neck/internal sphincter resistance (intact T11-L2 sympathetics). • non-contractile bladder with leakage from overflow. (NB. May also be sequelae to recurrent bladder overdistensions.)

Figure 2 – The European Association of Urology (EAU) – Madersbacher functional classification system based on urodynamic and clinical findings*



**Adapted from Madersbacher H. The various types of neurogenic bladder dysfunction: an update of current therapeutic concepts. Paraplegia. 1990; 28(4):217-29.*



CIC: Clean intermittent catheterization

DLPP: Detrusor leak point pressure

UDS: Urodynamic study

Penatalaksanaan

1. *Intermittent catheterization*
2. *Medication*
3. *Botulinum Toxin A (BTX-A) injection*
4. *Neuromodulasi*
5. *Urinary tract reconstruction surgery*
6. *Terapi terbaru*

Intermittent chateterization

- Menggunakan intermittent self atau third-party catetherization → dilakukan 4 – 6 kali / hari dgn kateter ukuran 12-14.
- Saat dilakukan kateterisai diharapakan volum urin < 400mL

Farmakologi

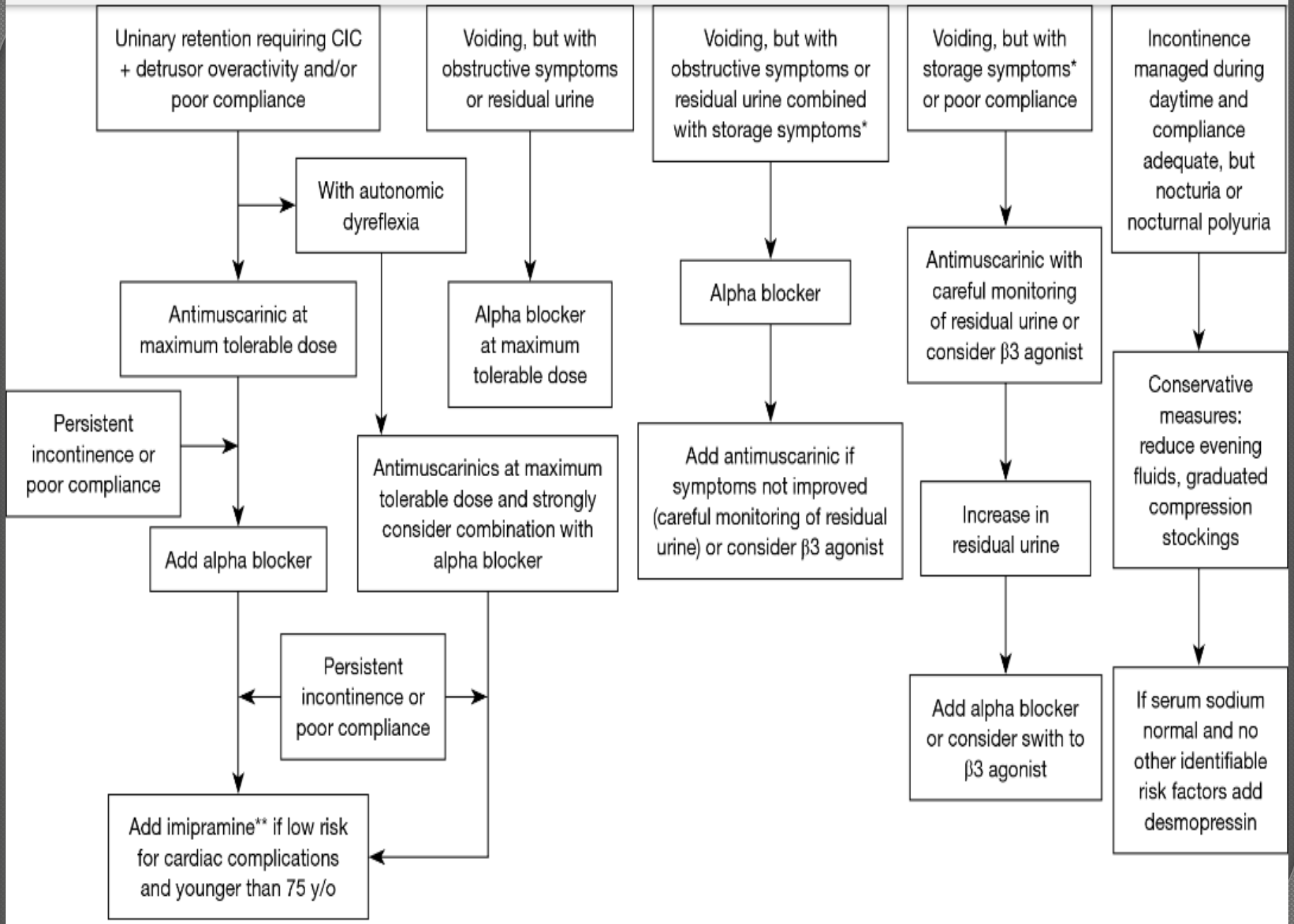
- Anti muscarinic → ditoleransi dgn baik, aman utk long term treatment. Solifecanin oral → afinitas tinggi terhadap reseptor M3 muscarinic di vesika urinaria.
- Phospodiesterase Inhibitors (PDE51s) → bdasarkan pilot study mjadi terapi alternatif atau terpi adjunctive thdp anti muscarinic.
- ß3-adrenergic reseptor agonist → digunakan utk pasien *overactivity bladder* (OAB) → dikombinasi dgn anti muscarinic
- α blocker → non selective dan selective α blocker → menurunkan resistensi vesika urinaria, residual urine, autonomic dysreflexia.

TABLE 3 – A summary of pharmacological and non-pharmacological options to manage various types of lower urinary tract dysfunction following spinal cord injury are listed.

Detrusor Hyperreflexia
• Oral anticholinergic medications (e.g. Oxybutynin, Tolterodine, Solifenacin). (Comment: Transdermal Oxybutynin may also be used). • Denervation (typically using intravesical Botulinum toxin). • Sacral deafferentation (surgical division of sacral posterior roots). This may sometimes be required to control detrusor hyperreflexia with associated AD. Comment: neuromodulation shows some promise, but requires further study.
Low Bladder Compliance/Capacity
• Anticholinergic medications (as above). • Bladder augmentation surgery ('Clam' ileocystoplasty). • Ileal conduit.
Bladder Neck/Sphincter Insufficiency
• Alpha agonist medication (e.g. Imipramine). • Peri-urethral injection of macroplastique polymer. • Sub-urethral sling/taping procedure. • Artificial sphincter (inflatable cuff) device.
Bladder Neck/Sphincter Obstruction
• Alpha adrenergic antagonist medications (e.g. Phenoxybenzamine, Prazosin). • Spasmolytic agents (e.g. Baclofen, Diazepam, Botulinum toxin injection). • Local anaesthetic (Xylocaine gel per urethra). • External sphincterotomy/urethral wall stent. • Prostatectomy/urethrotomy (for mechanical causes such as benign prostatic hypertrophy or urethral stricture).

Table 2 Alpha blocker medications

Medication	Dose range	Side effects
Alpha blockers	-	Rhinitis, postural hypotension, dizziness, abnormal ejaculation
Alfuzosin	5–10 mg daily	Less ejaculatory problems and less dizziness/postural hypotension
doxazosin	2–8 mg daily	Most dizziness and postural hypotension – need dose escalation
Terazosin	2–10 mg daily	Most dizziness and postural hypotension – need dose escalation
Tamsulosin	0.4–0.8 mg daily	High rate of ejaculatory problems
Silosodin	8 mg daily	Lowest rate of ejaculatory and hypotension


Uninary retention requiring CIC + detrusor overactivity and/or poor compliance
Voiding, but with obstructive symptoms or residual urine
Voiding, but with obstructive symptoms or residual urine combined with storage symptoms*
Voiding, but with storage symptoms* or poor compliance
Incontinence managed during daytime and compliance adequate, but nocturia or nocturnal polyuria
With autonomic dyreflexia
Antimuscarinic at maximum tolerable dose
Alpha blocker at maximum tolerable dose
Alpha blocker
Antimuscarinic with careful monitoring of residual urine or consider β3 agonist
Conservative measures: reduce evening fluids, graduated compression stockings
Persistent incontinence or poor compliance
Add alpha blocker
Antimuscarinics at maximum tolerable dose and strongly consider combination with alpha blocker
Add antimuscarinic if symptoms not improved (careful monitoring of residual urine) or consider β3 agonist
Increase in residual urine
Persistent incontinence or poor compliance
Add alpha blocker or consider swith to β3 agonist
If serum sodium normal and no other identifiable risk factors add desmopressin
Add imipramine** if low risk for cardiac complications and younger than 75 y/o

Botulinum Toxin A (BTX-A) injection

- BTA-X → disuntikkan pd m.detrussor → scr teori berfungsi sementara memblok pre-synaptik melepaskan acetilkolin dari parasimpatik, dan menyebabkan paralisis otot halus detrussor.
- Toksin Botulinum → efek long lasting, tetapi denervasi kimianya reversibel.
- Pd pemeriksaan urodiamik → ditemukan perbaikan thp volum refleks, tekanan maksimum detrussor, *bladder compliance*, dan *maximum cytosmetric capacity*.

Neuromodulasi

- Sacral Neuromodulation (SNM) → minimal invasif, digunakan u/ LUT & *bowel dysfunction*.
- Pudendal Neuromodulation (PNS) → memberikan hasil yg bagus pd pasien dgn *dysfunctional voiding*.
- Percutaneus Tibial Nerve Stimulation (PTNS) → menggunakan adhesive skin-surface electrode yg diletakkan di kaki.
- Foot stimulation → menekan *bladder filling sensation dan* meningkatkan *bladder volume* pd orang normal.

Urinary Tract Reconstruction Surgery

- Augmentation Enterocystoplasty → bertujuan u/ menghasilkan reservoir dgn kapasitas besar, good compliance → dilakukan sigmoidocolocystoplasty terkadang dikombinasi dgn *uretral re-implantation*.
- Tissue-Engineering Bladder Augmentation → menggunakan *small intestine submucosa* (SIS) → terbukti meningkatkan fungsional vesika urinaria.
- Artificial Urinary Sphincter (AUS) →pasien dgn NB mempunyai resitensi vesika urinaria yg rendah → AUS memungkinkan terjadinya *spontaneus voiding*.

Terapi Baru

- Stem Cell Transplantation →sel neuron & sel glia matur tidak dpt beregenerasi → mk ditransplantasikan neural progenitor cells u/ merangsang perbaikan fungsi vesika urinaria dgn jalan terjadinya regenerasi pd area yg cedera.
- Gene therapy → terapi gen ini bertujuan agar terekspresinya kynurenine yg merupakan antagonis *N-methyl-D-aspartatereceptors* (NMDARs).

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TERIMAKASIH