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Guidelines

EAU Guidelines on Neurogenic Lower Urinary Tract Dysfunction

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Abstract

Context: Most patients with neurogenic lower urinary tract dysfunction (NLUTD) require life-long care to maintain their quality of life (QoL) and to maximise life expectancy.

Objective: To provide a summary of the 2008 version of the European Association of Urology (EAU) guidelines on NLUTD and to assess the effectiveness of currently available diagnostic tools, particularly ultrasound imaging and urodynamics.

Evidence acquisition: The recommendations provided in the 2008 EAU guidelines on NLUTD are based on a review of the literature, using online searches of Medline and other source documents published between 2004 and 2007. A level of evidence and/or a grade of recommendation have been assigned to the guidelines where possible.

Evidence synthesis: NLUTD encompasses a wide spectrum of pathologies, and patients often require life-long, intensive medical care to maximise their life-expectancy and to maintain their QoL. Treatment must be tailored to the needs of the individual patient and, in many cases, involves a multidisciplinary team of experts. Timely diagnosis and treatment are essential if irreversible deterioration of both the upper and lower urinary tracts are to be avoided. Therapeutic decisions are made on the basis of a comprehensive medical assessment, including urodynamics to identify the type of dysfunction. Advances in investigative technologies have facilitated the noninvasive and conservative management of patients who have NLUTD.

Conclusions: The diagnosis and treatment of NLUTD, which is a highly specialised and complex field involving both urology and medicine, requires up-to-date expert advice to be readily available. The current guidelines are designed to fulfil this need.

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1. Introduction

Before the 1980s, considerable morbidity was associated with renal failure in patients with neurogenic lower urinary tract dysfunction (NLUTD) [1,2]. Most patients with NLUTD require life-long care to maintain their quality of life (QoL) and to maximise life expectancy. Significant technologic developments that have occurred over the last 30 yr have helped to achieve these goals.

The European Association of Urology (EAU) Guidelines Working Panel for NLUTD prepared this overview of the 2008 EAU guidelines on NLUTD, presented at the 23rd Annual EAU Congress [3], to enable urologists to incorporate evidence-based management of NLUTD into their clinical practice.

2. Evidence acquisition

A detailed literature search for high-quality data published between 2004 and 2007 was carried out using Medline and other source documents (eg, textbooks and medical and scientific Web sites).

Where possible, the panel has used a three-tier system (A–C) [4] to grade treatment recommendations to assist clinicians in determining the validity of a recommendation.

No data on the prevalence of NLUTD in the general population are available. Data are available, however, on the prevalence of underlying causative conditions and the risk that these conditions pose for the development of NLUTD, although generally this information comes from studies involving only small sample sizes.

The limited availability of randomised, controlled trials plus the fact that a considerable number of treatment options involve surgical intervention were further drawbacks. In areas in which conclusive data are lacking, this paper presents a consensus view. Because no consistent level of evidence (LE) is available for most of the diagnostic

procedures, grades of recommendations (GRs) are provided based on expert opinion.

The terminology used and the diagnostic procedures outlined in these guidelines follow the recommendations for the investigation of the lower urinary tract (LUT) published by the International Continence Society (ICS) [5,6] (Table 1).

3. Evidence synthesis

3.1. Risk factors and epidemiology

All central and peripheral neurologic disorders carry a high risk of causing functional disturbances of the urinary tract.

3.2. Classification

Several classification systems have been proposed for NLUTD. The recommendations for a functional classification for motor function are based on urodynamic and clinical findings [7] (Fig. 1).

3.3. Timing of diagnosis and treatment

In both congenital and acquired NLUTD, early diagnosis and treatment are essential because irreversible changes within the LUT may occur, even when the related neuropathologic signs are normal [8,9]. Additionally, NLUTD can, by itself, be the presenting feature of neurologic pathology [10,11].

3.4. Diagnosis

Diagnosis of NLUTD should be based on a comprehensive assessment of neurologic and non-neurologic conditions. Initial patient assessment should include a detailed history, physical examination, and urinalysis.

Table 1 – Definitions useful in clinical practice*

Catheterisation, indwelling	Emptying of the bladder by a catheter that is introduced (semi-)permanently
Intermittent catheterisation (IC)	Emptying of the bladder by a catheter that is removed after the procedure, mostly at regular intervals
Aseptic IC	The catheters remain sterile, the genitals are disinfected, and (disinfecting) lubricant is used
Clean IC	Disposable or cleansed reusable catheters, genitals washed
Sterile IC	Complete sterile setting, including sterile gloves, forceps, gown, and mask
Intermittent self-catheterisation	Performed by the patient
Filling rate, physiologic	Below the predicted maximum calculated as body weight kilograms/4 in millilitres per second
Lower motor neuron lesion	Lesion at or below the S1–S2 spinal cord level
Rehabilitation, LUT	Nonsurgical nonpharmacologic treatment for LUT dysfunction
Upper motor neuron lesion	Lesion above the S1–S2 spinal cord level
Voiding, balanced: in patients with NLUTD (postvoid residual <80 ml or <20% of bladder volume)	Voiding with physiological detrusor pressure and low postvoid residual
Voiding, triggered	Voiding initiated by manoeuvres to elicit reflex detrusor contraction by exteroceptive stimuli
Detrusor leak-point pressure	Lowest value of detrusor pressure at which leakage is observed in the absence of abdominal strain or detrusor contraction

LUT = lower urinary tract; NLUTD = neurogenic lower urinary tract dysfunction.

* Modified from Abrams et al [6].

EAU-Madersbacher classification system

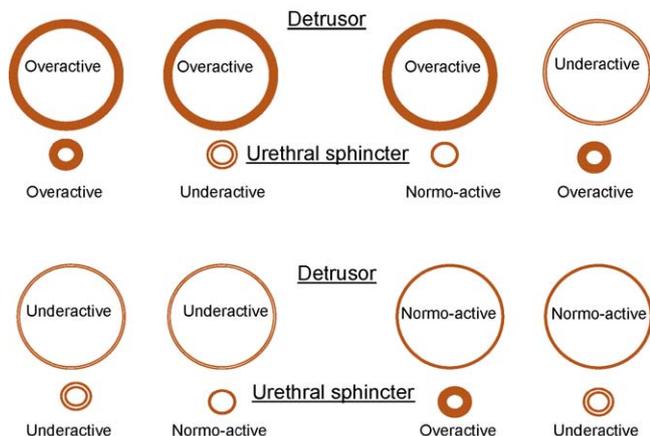


Fig. 1 – The European Association of Urology (EAU)–Madersbacher classification system. Adapted from Madersbacher et al [7].

3.4.1. Patient history

An extensive general and specific history is mandatory and should concentrate on past and present symptoms and disorders of the urinary tract and bowel and on sexual and neurologic function. Special attention should be paid to possible warning signs and symptoms (eg, pain, infection, haematuria, and fever) that warrant further investigation.

The history should include the following items:

- Acquired or congenital neurologic conditions
- Neurologic symptoms (somatic and sensory), including their onset, evolution, and any treatment
- Spasticity or autonomic dysreflexia (lesion above thoracic sixth vertebra)
- Mental status and comprehension
- Prior surgery
- Medications
- Mobility and hand function
- Socioeconomic situation.

3.4.2. Physical examination

In addition to a detailed patient history and a general examination, neurologic status should be described as completely as possible. All sensations and reflexes in the urogenital area must be tested, and detailed testing of the anal sphincter and pelvic floor functions must be performed (Fig. 2). Availability of this clinical information is essential for the reliable interpretation of subsequent diagnostic investigations.

3.4.3. Urodynamic tests

A bladder diary should be recorded for at least 2–3 d [5]. Possible pathologic findings include high voiding frequency, very small or very large voided volumes, nocturnal voiding, urgency, and incontinence.

Uroflowmetry and ultrasound assessment of postvoid residual should be repeated at least two or three times in patients who are able to void [5]. Possible pathologic findings include low urine flow rate, low voided volumes, intermittent flow, hesitancy, and large postvoid residual.

3.4.4. Invasive urodynamic studies

Invasive urodynamic studies use mandatory assessment tools to determine the exact type of NLUTD (Table 2). Although referred to as *invasive*, these studies are generally associated with low complication rates [12].

Filling cystometry is the only procedure that quantifies the filling function of the bladder; however, when filling cystometry is used alone, the results have limited significance. Possible pathologic findings include detrusor overactivity, low bladder compliance, detrusor/sphincter dyssynergia (DSD), abnormal bladder sensation and other sensations (eg, autonomic dysreflexia), and incontinence.

Measurement of detrusor leak-point pressure (DLPP) has limited diagnostic value; it is not recommended as a stand-alone test. A high DLPP warrants further investigation with video-urodynamics.

Pressure–flow studies used to test the function of the LUT must also be made during the voiding phase

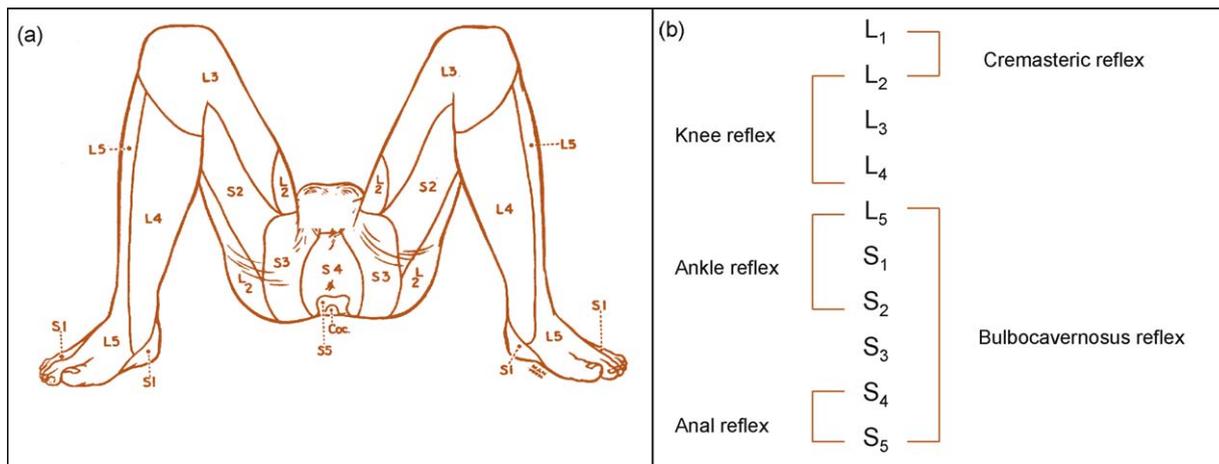


Fig. 2 – The neurologic status of a patient with neurogenic lower urinary tract dysfunction (NLUTD) must be described as completely as possible: (a) dermatomes of spinal cord levels L2–S4; (b) urogenital and other reflexes in the lower spinal cord.

Table 2 – Guidelines for urodynamics and uro-neurophysiology tests in neurogenic lower urinary tract dysfunction (NLUTD)

Guidelines for urodynamics and uro-neurophysiology tests	GR
Urodynamic investigation is necessary to document the (dys-)function of the LUT [10].	A
The recording of a bladder diary is advisable.	B
Noninvasive testing is mandatory before invasive urodynamics are planned.	A
Video-urodynamics are currently the preferred method for invasive urodynamics in patients with NLUTD. If this method is not available, then a filling cystometry continuing into a pressure–flow study should be performed.	A
For standard urodynamic testing, a physiologic filling rate (see Table 1; eg, not faster than 20 ml/min) and body-warm fluid must be used.	A
Specific uro-neurophysiologic tests and provocative manoeuvres (eg, fast-filling cystometry with cooled saline [the <i>ice-water test</i>], coughing, tapping, and anal stretch) are elective procedures [10,12].	C

GR = grade of recommendation; LUT = lower urinary tract.

whenever possible. Possible pathologic findings include detrusor underactivity or acontractility, DSD, an incompetent urethral closure mechanism, nonrelaxing urethral sphincter obstruction, and increased postvoid residual.

Video-urodynamics combine filling cystometry and pressure–flow studies with radiologic imaging. Possible pathologic findings include all of the conditions described above under filling cystometry and pressure–flow studies plus morphologic abnormalities of the urinary tract. Special attention is given to demonstrable vesico-ureteral reflux. Currently, video-urodynamics are considered to provide the most comprehensive information for evaluating NLUTD [5].

Electromyography (EMG) is a semiquantitative measure of pelvic-floor activity that can be used to detect DSD and pelvic-floor relaxation disorders.

3.4.5. Specific uro-neurophysiologic tests

Specific uro-neurophysiologic tests form part of the neurologic work-up (Table 3) and include the following items:

- Electromyogram of pelvic-floor muscles, urethral sphincter, and/or anal sphincter
- Nerve-conduction studies of the pudendal nerve
- Reflex latency measurements of bulbocavernosus and anal reflex arcs
- Evoked responses from clitoris or glans penis
- Sensory testing of the bladder and urethra.

Table 3 – Characteristic findings in neurogenic lower urinary tract dysfunction*

Filling phase
Increased, decreased, or absent bladder sensation
Vegetative nonspecific sensations
Low level of bladder compliance
High level of capacity bladder
Detrusor overactivity, spontaneous or provoked
Incompetent urethral closure mechanism
Voiding phase**
Acontractile or underactive detrusor
Bladder-outlet obstruction
Detrusor/sphincter dyssynergia
Nonrelaxing urethral sphincter obstruction

* Modified from Abrams et al [6].

** These signs warrant further neurologic evaluation because lower urinary tract dysfunction may be the presenting symptom of a neurologic disease [8].

3.5. Treatment

Treatment of NLUTD aims to protect the upper urinary tract and to improve continence, QoL, and, whenever possible, LUT function. In patients with NLUTD, preservation of upper urinary tract function is essential [2,13]. In patients with a high detrusor pressure in the filling phase, the principal aim of treatment is conversion of an overactive, high-pressure bladder into a low-pressure reservoir, even if this should result in a high postvoid residual [13]. Other considerations when planning treatment of NLUTD should include the patient's condition, potential complications, technical aspects, and cost effectiveness [13]. The patient's QoL is a prime consideration when making any treatment decision.

3.5.1. Conservative treatment

There are few prospective, randomised, controlled studies of the medical management of NLUTD.

3.5.1.1. Drug treatment for neurogenic detrusor overactivity. A single optimal medical therapy for neurogenic detrusor overactivity (NDO) is not yet available. Antimuscarinic agents are currently the most widely used treatment, although most of the available drugs have not been registered for the treatment of this patient population (Table 4). Patients with a neurogenic bladder disorder usually need a higher dose of antimuscarinics than patients with idiopathic detrusor overactivity [14] (LE: 1b; GR: A); however, higher doses are associated with a higher rate of side-effects [15]. Antimuscarinic agents can also be given intravesically [16] (Table 4).

3.5.1.2. Drug treatment for neurogenic detrusor underactivity. There is no evidence of effective drug treatment for neurogenic detrusor underactivity [13] (LE: 2a; GR: B).

3.5.1.3. Drug treatment to decrease bladder-outlet resistance. Selective and nonselective α -blockers have been partially successful in decreasing bladder-outlet resistance, residual urine, and autonomic dysreflexia [13] (LE: 2a; GR: B).

3.5.1.4. Catheterisation. Intermittent catheterisation (IC) (ie, self-catheterisation or third-party catheterisation) [17] is the gold standard for the management of NLUTD [13].

Sterile IC significantly reduces the risk of urinary tract infection (UTI) and/or bacteriuria [13,17,18] compared with

Table 4 – Antimuscarinic treatment for neurogenic detrusor overactivity

Drug	References	Comment	LE	GR
Oxybutynin	Block et al [38], Granata et al [39]	–	1b	A
Trospium chloride	Dykstra and Sidi [36], Wilson et al [37]	–	1b	A
Tolterodine	Dykstra and Sidi [36], Ströher and Pannik [42]	–	1b	A
Propiverine	Granata et al [39], Ströher et al [43]	–	1b	A
Darifenacin	–	No data as yet	–	–
Solifenacin	–	No data as yet	–	–
Fesoterodine	–	No data as yet	–	–

LE = level of evidence; GR = grade of recommendation.

clean IC. Sterile IC, however, cannot be used routinely; aseptic or clean IC are feasible alternatives [19,20]. Compared with clean IC, aseptic IC provides significant benefit in reducing the potential for contamination [19]. Inadequate education and the inherently greater risk of UTI in patients with NLUTD contribute to the risk of infection [13,20]. On average, for catheterisation, a 12–14 French catheter is needed four to six times per day. Less frequent catheterisation results in higher bladder-storage volumes and an increased risk of UTI [20]. More frequent catheterisations increase the risk of cross-infection [20].

Indwelling transurethral catheterisation and, to a lesser extent, suprapubic cystostomy should be avoided because they are risk factors for UTI and for significant long-term complications [13,21–23]. If indwelling catheters have to be used, empirical evidence and expert opinion suggest that silicone catheters have advantages over latex catheters [24].

3.5.1.5. Assisted bladder emptying. Triggered reflex voiding is not recommended because there is a risk of pathologically elevated bladder pressures. Only in the case of absence of this reflex or in the case of a reflex reduced as a result of surgery should outlet obstruction be an option [13].

Bladder compression techniques to expel urine (Crede) and voiding by abdominal straining (Valsalva manoeuvre) create high pressures and are potentially hazardous, and their use should be discouraged [13].

3.5.1.6. Rehabilitation. LUT rehabilitation includes prompted voiding, timed voiding (bladder training), and lifestyle modification [14]. In selected patients, pelvic-floor muscle exercises, pelvic-floor electrostimulation, and biofeedback might be beneficial [25].

3.5.1.7. External appliances. External appliances may be the most effective remedy for some patients. Social continence for the incontinent patient can be achieved using an appropriate method of urine collection [13]. Condom catheters or pads can offer a reliable solution. In both cases, the patient must be monitored closely because there is a risk of infection [13]. Because penile clamp is associated with high pressure on the urethral tissue and will reduce penile blood flow, it should not be used routinely [26].

3.5.2. Minimally invasive treatment

3.5.2.1. Botulinum toxin A injections in the bladder. Botulinum toxin A causes a long-lasting (up to 9 mo), reversible, chemical denervation [27,28]. Botulinum toxin A has been proven to be

effective in small, randomised, placebo-controlled trials in NLUTD [29,30]. Repeated injections can be given without loss of efficacy [28,31]. Generalised muscle weakness is an occasional adverse effect [28,31]. Histologic studies have not found ultrastructural changes in bladder muscle after injection [32]. Botulinum toxin A is currently only available on a named-patient basis in every European country except Switzerland, where it has regulatory approval.

3.5.2.2. Intravesical vanilloid treatment. The vanilloids, capsaicin, and resiniferatoxin desensitise the C-fibres, thus temporarily decreasing detrusor overactivity. Resiniferatoxin and capsaicin, however, have limited clinical efficacy compared to botulinum toxin A injections into the detrusor [33,34].

3.5.2.3. Bladder-neck and urethral procedures (see section 3.5.3.3). Reduction of the bladder-outlet resistance to protect the upper urinary tract can be achieved by sphincterotomy [35] or by chemical denervation of the sphincter using botulinum toxin A [36]. Incontinence may result and can be managed using external devices. Insertion of urethral stents is not recommended because this procedure is associated with substantial complication and reintervention rates [37]. Increasing bladder-outlet resistance using bulking agents, urethral inserts, or alternative appliances is not recommended for long-term treatment [38] (LE: 2a; GR: B).

3.5.2.4. Neurogenic detrusor overactivity and reflux. Vesico-ureteral reflux should be managed by lowering intravesical pressure. If reflux is persistent, intervention using bulking agents or ureteral reimplantation can be considered [39,40].

3.5.3. Surgical treatment

3.5.3.1. Overactive detrusor. Bladder augmentation (eg, clam cystoplasty) is indicated for an overactive detrusor when less invasive procedures have failed [41,42] (Fig. 3).

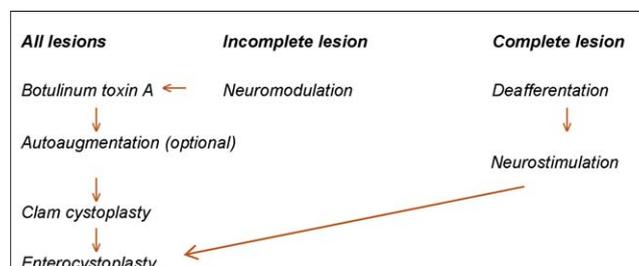
**Fig. 3 – Surgery for neurogenic detrusor overactivity.**

Table 5 – Minimum follow-up required in patients with neurogenic lower urinary tract dysfunction*

Investigation**	Frequency	GR
Urinalysis	At least once every 6 mo	A
Ultrasound of the upper urinary tract, bladder status, and postvoid residual	Every 6 mo	A
Physical examination, blood biochemistry, and urine microbiology	Annually	A
Video-urodynamic investigations in patients without detrusor overactivity and with normal bladder compliance	Every 2 yr	A
Video-urodynamic investigations in patients with detrusor overactivity and/or low bladder compliance	At least once per year	A

GR = grade of recommendation.
 * Grades of recommendation assigned on basis of panel consensus.
 ** The need for detailed special investigations must be determined on the basis of the patient's risk profile, but they should, where indicated, include a video-urodynamic study, which should be carried out in an institution with neurourologic expertise.

Alternative options include autoaugmentation (myomec-tomy) [43]; dorsal rhizotomy, with or without sacral anterior root stimulation (SARS) (complete lesions); and neuromodulation (incomplete lesions) [44,45]. Substitution with either continent [46] or incontinent diversion [47] is indicated for the small, contracted, noncompliant bladder [46].

3.5.3.2. *Underactive detrusor.* SARS (complete lesions) and sacral neuromodulation (incomplete lesions) [44,45] are effective in selected patients (LE: 2; GR: B).

3.5.3.3. *Sphincter insufficiency (underactive urethra).* The artificial urinary sphincter is the preferred treatment for patients with NLUTD [48] (LE: 2; GR: B). Alternative procedures are the placement of a bladder-neck sling or a midurethral sling [49,50] (LE: 3; GR: B). Various materials have been used for a midurethral sling [51].

Procedures to treat sphincter incompetence are suitable only when the detrusor activity is, or can be, controlled and there is no significant associated vesico-ureteral reflux. Simultaneous bladder augmentation and artificial sphincter implantation is an option in patients with neurogenic disorders [52].

3.6. Quality of life

QoL is a very important aspect of the global management of a patient who has NLUTD. Restoration and maintenance of the patient's QoL, as much as possible, should be one of the major aims of treatment. QoL should be integral to the evaluation of LUT symptoms in patients with NLUTD and also when considering any type of treatment for neurogenic bladder dysfunction [53] (LE: 2a; GR: B). QoL can be assessed using Qualiveen, a specific tool for patients with spinal cord lesions and those suffering from multiple sclerosis and visual analogue scale (VAS) [54]. Generic short-form health survey (SF-36) tools or specific questionnaires like the Urinary Incontinence Quality of Life Scale (I-QOL) to assess incontinence can also be used [55] (LE: 2a; GR: B). Currently, there are no disease-specific outcome measures for the assessment of health-related QoL in patients with NLUTD.

3.7. Follow-up

NLUTD is an unstable condition which manifests itself with considerable variability, even within a relatively short time

frame. Meticulous, regular follow-up is essential [42]. Individualised patient follow-up is imperative to safeguard QoL and life expectancy. The underlying pathology and the state of the urinary tract dictate the frequency of follow-up required. Minimum follow-up is outlined in Table 5.

4. Conclusions

NLUTD is a multifaceted pathology. Extensive investigation and a precise diagnosis are required before the clinician can initiate individualised therapy. Treatment must take into account the patient's medical and physical condition and expectations with regard to his or her future social, physical, and medical situation.

This paper provides a summary of the 2008 European Association of Urology (EAU) guidelines on neurogenic lower urinary tract dysfunction (NLUTD). More detailed information and a complete reference list are available in the full-text version of the guidelines, which can be found on the Web site of the EAU (<http://www.uroweb.org/nc/professional-resources/guidelines/online/>). The full text version of the NLUTD guideline is also available on the EAU's Web site (<http://www.uroweb.org/nc/professional-resources/guidelines/online/>).

Author contributions: Manfred Stöhrer had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Study concept and design: Stöhrer, Blok, Castro-Diaz, Chartier-Kastler, Del Popolo, Kramer, Pannek, Radziszewski, Wyndaele.

Acquisition of data: Stöhrer, Blok, Castro-Diaz, Chartier-Kastler, Del Popolo, Kramer, Pannek, Radziszewski, Wyndaele.

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