# Contemporary methods of urinary system evaluation in patients after spinal injury complicated by neurological deficits: Diagnostics of the upper urinary tract

## Współczesne metody oceny układu wydalniczego u osób po urazie kręgosłupa powikłanym zaburzeniami neurologicznymi – diagnostyka górnych dróg moczowych

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**Key words**
spinal injury, neurological deficits, urinary system, urinary tract

**Abstract**
Introduction: Morbidity and mortality related to urinary tract diseases in patients after spinal injury with neurological disturbances (SIND) are modifiable if prompt and rational diagnostics and therapy are implemented in comprehensive care. SIND increases the risk of urinary tract damage resulting from neurogenic bladder dysfunction, sequels of patient's immobilisation, nephrotoxic effect of pharmacotherapy, necessity of bladder catheterisation. Severe damage to the urinary system resulting from reflux, urolithiasis, hydronephrosis, recurrent pyelonephritis can occur both during the early and the late phase following SIND. The risk of urinary tract cancer is markedly increased in SIND patients. The natural history of urinary tract diseases in SIND patients might be changed. The course of the disease can be scant in symptoms and signs until late stages.
Study design: Overview of scholarly literature.
Aim of the study: Presentation and analysis of clinical usefulness of modern tests applied in diagnostics of the urinary tract function in SIND patients. We discussed appropriateness and clinical usefulness of imaging and functional procedures of the upper urinary tract evaluation with special emphasis on basic laboratory tests, modern methods of glomerular filtration rate (GFR) assessment in SIND patients, as well as on the traditional and modern imaging studies.
Conclusions: Modern comprehensive care of a patient with SIND, both at the early and late stage following spinal injury, should comprise systematic monitoring of renal function. Efficacious diagnosis is based on meticulous clinical examination. Auxiliary tests are performed according to their availability and the anticipated clinical relevance. First line diagnostic tests should comprise non-invasive techniques. Systematic and credible GFR assessment is indicated in SIND patients. Tests of choice include: 51CrEDTA or 99mTcDTPA clearance, assessment of cystatin-C level, as well as routine imaging studies of the kidneys such as renal radioisotope scanning and ultrasound examination. Urography and computed tomography may serve as auxiliary imaging techniques.

**Słowa klucze**
uraz kręgosłupa, zaburzenia neurologiczne, układ wydalniczy, drogi moczowe

**Streszczenie**
Wstęp: Chorobowość i śmiertelność z powodu schorzeń układu wydalniczego w populacji pacjentów po urazie kręgosłupa z zaburzeniami neurologicznymi (UKPZN) są czynnikami modyfikowalnymi pod warunkiem zastosowania wczesnej diagnostyki i odpowiedniej terapii we wczesnym stadium tych schorzeń. Przebycie UKPZN podnosi ryzyko uszkodzenia układu wydalniczego w wyniku neurogennych zaburzeń motoryki dróg moczowych, konsekwencji unieruchomienia pacjenta, neurotoksycznego efektu leków, konieczności cewnikowania pęcherza. Ciężkie uszkodzenia dróg moczowych w następstwie refluksu, kamicy dróg moczowych, wodonercza, odmiedniczkowego zapalenia nerek, mogą wystąpić w zarówno we wczesnym, jak i odległym okresie po UKPZN. U osób z UKPZN zwiększone jest ryzyko nowotworów dróg moczowych. Schorzenia układu wydalniczego w licznych przypadkach UKPZN mają podstępny, skąpoobjawowy przebieg.

Authors' contribution: A – project of the study, work; B – collection of the data, information; C – statistical analysis; D – data interpretation; E – preparation of the manuscript; F – literature query; G – obtaining funds

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Cel pracy: Przedstawienie i analiza użyteczności współczesnych testów diagnostycznych wykorzystywanych przy rozpoznawaniu schorzeń górnych dróg moczowych po UKPZN. Omówiono celowość i przydatność kliniczną testów oceniających morfologię i funkcję górnych dróg moczowych, ze szczególnym uwzględnieniem podstawowych badań laboratoryjnych, współczesnych sposobów oceny przesączania kłębuszkowego u osób po UKPZN, oraz tradycyjnych i współczesnych badań obrazowych.
Projekt pracy: Przegląd literatury
Wnioski: Współczesna kompleksowa opieka nad pacjentem we wczesnym i odległym okresie po UKPZN powinna obejmować regularne i systematyczne monitorowanie czynności nerek. Podstawą skutecznej diagnostyki jest badanie przedmiotowe i podmiotowe. Na wybór dodatkowych technik diagnostycznych ma wpływ ich dostępność i spodziewana przydatność kliniczna. Jeśli to jest możliwe w diagnostyce należy w piewszym rzędzie wykorzystywać techniki nieinwazyjne. U osób po UKPZN istnieją wskazania do regularnej przesiewowej oceny przesączania kłębuszkowego (np. klirens 51CrEDTA lub 99mTcDTPA czy badanie poziomu cystatyny C) oraz rutynowe badanie obrazowe nerek takie jak renografia czy USG. Badaniami uzupełniającymi mogą być urografia i tomografia komputerowa jamy brzusznej.

## Introduction

Typical consequences of spinal injury with neurological disturbances (SIND) include disturbances of both upper (kidneys, ureters) and lower (urinary bladder, urethra) urinary tract. The initial cause of disturbances is occurrence of signs of autonomic or automatic bladder following injury of the spinal cord, the cone or the cauda equina.

Most frequent causes of kidney damage in a person with SIND include urinary tracct infections, urinary reflux, lithiasis of the urinary tract, hydronephrosis, nephrotoxic effects of drugs (e.g. amine-glycosides[1]), or secondary amyloidosis.

Bacteriuria is detected in approximately 80% of patients after SIND2. Neurogenic disturbances of urinary outflow and urolithiasis increase the risk of transformation of symptoms-free bacteriuria into acute pyelonephritis (PN). Signs of PN are sometimes difficult to differentiate from urinary tract infections without involvement of the kidneys because of possible absence of the characteristic pain, disturbances of thermoregulation. Acute PN occurs in 1/3 of persons after SIND[2]. Chronic PN is an interstitial nephropathy, often of a mild course that can lead to gradually progressing renal failure.

Patients with neurogenic dysfunction of the urinary tract require planned monitoring of renal function life-long because of the frequently treacherous, sparsely symptomatic course of initial phases of urinary tract diseases.

This work is restricted to description of diagnosing signs of diseases typically resulting from SIND. Presence of concomitant diseases such as diabetes mellitus, prostate hypertrophy, nephropathies of various origin or past traumatic injuries of the urinary system alter the natural course of complications and additionally complicate the clinical picture.

## Aim of the study

The aim of the work is to describe contemporary methods of imaging and functional diagnostic studies of the upper urinary tract as a part of complex care of patients with SIND.

## History

When starting to evaluate the function of the urinary system in a SIND person, information about the method of bladder emptying should be obtained, e.g. referring to frequency of catheterisation and conformance to the principles of maintenance of aseptic conditions. It is worth answering the question whether the applied method is acceptable for the patient and what inconveniencies it is associated with. Information on daily intake and excretion of fluids, diurnal distribution of fluids taken orally, patient's sensation of urgency, possibilities of initiation and control of micturition, presence and type of pain associated with urination, time spent on emptying the bladder, symptoms of urinary incontinence and disturbances related to autonomic dysreflexia (rises in blood pressure, paroxysmal headaches, generalised sweating) is of great importance. It is also very important to obtain information about the time of the injury, type and localisation of the lesion of the nervous system. Clinical picture of urinary bladder dysfunction immediately following spinal cord injury, during the spinal shock phase, is distinct from that of the later phase. Different disturbances result from spinal cord injury and damage to the cone or the cauda equina. Symptoms are usually too unspecific to allow selection of an effective therapy[3]. Questions pertaining to past medical history, past and current medication, functional capability (effectiveness of handgrip, agility in moving from one place to another in the sitting position, agility in changing body position, ability to maintain balance during sitting – associated with independence in performance of bladder emptying activities) are all an important source of information. It should be remembered that post-SIND patients can develop marked renal failure when having serious diseases of the urinary tract and that this failure may be manifested only by scarce specific symptoms. Acute hydronephrosis typically associated with strong pain due to stretching of the renal capsule can have a non-painful course in a person with sensation disturbances. Slowly progressing hydronephrosis may cause only mild pain even in patients with preserved sensation[4]. Renal failure usually induces unspecific ailments such as lack of appetite, nausea, vomiting, disturbances of consciousness and oedema.

## Medical examination

Detailed medical examination enables detection of numerous more or less specific symptoms of renal dysfunction. Attention should be drawn to mental status, state of arousal and consciousness, body temperature, skin and mucosa colour, presence and localisation of oedema. It is helpful to assess patient's weight to evaluate collection of fluid in the organism. More detailed description of medical examination is beyod the scope of this article.

Complete patient management following SIND should consider determination of the level and degree of motor and sensory deficit with special attention paid to functioning of the dermatomes and myotomes of the sacral segment (sensation in the perineal region, tone and presence of voluntary constriction of the sphincter ani muscle). Cutaneous reflexes important for the assessment of innervation of the lower urinary tract include: the cremaster reflex (L1-L2), bulbocavernosus reflex and the anal reflex (S2-S4). Absence of these reflexes may be indicative of a lesion within the pyramidal tract or the peripheral nervous system. Absence of the bulbocavernosus reflex is not a specific sign, because this reflex is present only in 70-85% of healthy persons[3].

Per rectum examination can provide preliminary information about general size of the prostate, however, it does not allow drawing conclusions as to the degree to which prostate hypertrophy constitutes a barrier in urine outflow and bladder emptying[3].

### Blood count and electrolyte levels

Anaemia occurs in the majority of patients with chronic renal failure and is associated with reduced erythropoietin level. Sodium concentration is usually maintained within normal limits in mild or moderate renal failure, without signs of oliguria. In advanced renal failure, potassium level increases when oliguria or disturbances in aldosterone secretion occur. Impaired cellular reuptake of potassium additionally contributes to those changes[5].

In chronic renal failure, hypocalcaemia can occur as a result of disturbed calcitriol synthesis and chronic hyperphosphataemia. Hypercalcaemia in post-SIND patients is most frequently associated with immobilisation and enhanced release of calcium from the bones but not with renal failure[6]. Increase in calcium blood concentration can also occur when renal failure is treated with oral calcium carbonate or acetate to bind phosphates delivered with the food, especially when calcitriol is concomitantly used.

In case of dysfunction of more distal part of the nephron, e.g. in nephropathy due to amine-glycosides intake, loss of magnesium with urine occurs that can secondarily lead to hypokalaemia and hypocalcaemia[1].

## General urine examination

### Diurnal urine volume

Polyuria can be a sequel of a lower capability of urine concentration resulting from dysfunction of the distal renal tubule. Such phenomenon occurs e.g. as a result of nephrotoxic effects of amine-glycosides[1]. Polyuria of 3-11 litres suggests diabetes insipidus – insufficiency of the posterior hypophyseal lobe with secondary reduction in ADH level[7]. Diabetes insipidus is a rare complication of SIND at the cervical segment.

Oliguria (diuresis lower than 400 ml per day) is observed in dehydration and in advances stages of renal failure; however, this is an unspecific sign. Anuria (diurnal diuresis below 100 ml) most frequently accompanies shock and bilateral urinary tract occlusion. Normal or even slightly increased diurnal urine volume does not exclude unilateral or incomplete occlusion[8].

### Relative density (RD) and molality of urine

In patients with chronic PN, impairment of urine concentration is frequent. RD value higher than 1.020 g/cm$^3$ found in a random urine sample excludes presence of persistent disturbances of this type[8]. RD reduced to 1.0–1.003 g/cm$^3$ (which corresponds to osmolality of 50–200 mmol/kg) is a manifestation of diabetes insipidus of central origin[7,8]. RD of above 1.022 g/cm$^3$ is a risk factor for urolithiasis in patients after SIND[9].

Molality is a concentration of osmotically active particles. In urine containing no protein, molality expressed as mmol/kg $H_2O$ can be approximated based on RD by multiplying the second and the third digit following the dot in the RD value by 26.

### Urine pH

Assessment of urine pH is reliable only when the urine is sterile. Infection with *Proteus mirabilis* or other pathogenic organism synthesising urease leads to an increase in urine pH to values above 7.0–7.5. Determination of pH is required for reliability of urine sediment examination, because deformation of cellular elements of the sediment occurs in alkaline environment[10].

### Proteinuria

The test with indicator strips enables detection of albumins; however, it does not detect other proteins such as light immunoglobulin chains. The test is highly specific yet not quite sensitive allowing to determine presence of proteins in the urine at diurnal protein loss not lower than 300-500 mg. Diseases manifesting as massive albuminuria typically accompanied by oedema, include amyloidosis[11]. Proteinuria with albumins and globulins is observed e.g. in pyelonephritis and is accompanied by leukocyturia in such cases.

### Urine sediment

Urine should be inspected using a microscope not later than within 60 minutes following urine collection[12].

**1) Erythrocytes.** Blood loss with the urine exceeding 1 ml/l causes visible red discoloration of the urine. Presence of erythrocytes of a regular, round shape suggest an extra-renal bleeding, whereas erythrocytes of an altered shape (vesicle-like changes, partial loss of cellular membrane causing shape irregularity and size reduction) are most likely of renal origin. Most frequent causes of erythrocyturia include urolithiasis, hypertrophic bladder mucositis, urinary tract neoplasms and glomerulonephritis[13]. Transient haematuria is a relatively frequent phenomenon in young persons and usually does not reflect a disease of the urinary tract. Froom[14], who studied a group of 1000 persons aged 18-33 years found at least one episode of haematuria per year in 39% of the studied per-

sons and two or more such events in 16% of persons. In the group of 50-year old people, at least one episode of haematuria was observed in 10% of them during a 3-month follow-up period[15]. In elderly people, however, haematuria should not be neglected, as it can be the first sign of bladder cancer[3]; therefore, signs of bleeding from the urinary tract, especially of a larger and persistent one, require further diagnostic evaluation including use of invasive methods[16]. Transient haematuria accompanied by purulent urine and bacteriuria is most often associated with urinary tract infection. Haematuria can also be detected in a strip test. The strip test is a sensitive but not quite a specific method. False positive results can occur at urine pH above 9, contamination of the urine with sperm or oxidative agents used to wash the perineum. Falsely negative results are very rare[17].

**2) Leukocytes.** According to Stamm[18], purulent urine can be defined as presence of at least 8000 leukocytes in 1 ml of urine, which corresponds to presence of 2-5 leukocytes in large visual field during examination of centrifuged sediment. Clinically, it is important to differentiate aseptic leukocyturia (most frequently associated with tubular disease – e.g. in drug-induced nephropathies, urolithiasis, cancer, or contamination of the urine with vaginal secretion) from infection-induced leukocyturia. In case of infection, leukocyturia is not necessarily accompanied by bacteriuria, when the sample is taken after intake of anti-bacterial drugs or after urine contamination with an antiseptic agent[12].

**3) Casts.** Although random detection of casts is not necessarily indicative of renal disease, increased number of casts results most frequently from such diseases as renal tubular necrosis, pyelonephritis or nephrotic syndrome. These casts are sometimes difficult to distinguish from rolled-up leukocytes. The latter indicate a tubular-interstitial disease of the kidneys, acute pyelonephritis or post-infection glomerulonephritis[8]. Hyaline casts can occur as a result of fever or in case of damage to the renal parenchyma. Granular casts are a form of hyaline casts and usually occur in more severe forms of renal damage. Presence of erythrocyte casts is characteristic for glomerulonephritis. Waxy casts are typical for advanced stages of renal failure[10].

**4) Cristals.** Formation of crystals of calcium oxalate does not depend on urine pH, while calcium phosphate crystals occur only in alkaline urine. Ammonium-magnesium phosphate deposits can be precipitated only in cases of excessive ammonium production and increased urine pH reducing solubility of phosphates. Both of these situations occur during urinary tract infection with micro-organisms synthesising urease such as bacteria *Proteus* and *Klebsiella*. Partial, bilateral urinary tract obstruction bearing a risk of acute or chronic renal failure can, especially in post-SIND persons, have a symptom-free course, with normal or nearly normal urine examination, where mildly increased leukocyturia or erythrocyturia can only be observed[4].

## Microbiological urine examination

According to Biering-Sorenson, 81% of post-SIND patients experience at least one episode of urinary tract infection requiring antibiotic therapy during the first 5 years following the injury, while 22% of patients experience such infection 2-3 times per year, and 12% - 4-5 times a year[19]. *Escherichia coli* is the pathogen responsible for the majority of uncomplicated infections. Other pathogenic organisms include *Citrobacter*, *Enterobacter*, enterococci, *Pseudomonas aeruginosa*, *Staphylococcus aureus*, and fungi. Infections complicated with PN or urosepsis can be induced by bacteria other than the above, not infrequently demonstrating drug-resistance[20].

Collection of urine for microbiological study during morning hours creates greatest chance for detection of bacteria. Analysis of urine sample obtained by supra-pubic puncture is a gold standard in microbiological assessment of the urine[21]. Routine methods of urine collection for microbiological examination in post-SIND patients include catheterisation and spontaneous or forced micturition that are associated with a risk of contamination of the urine with bacteria located in the urethra or on the perineal surface.

Standard definition of significant bacteriuria of $10^5$ proliferation-capable bacteria per 1 ml or urine cannot be applied in all cases. Exclusion of faecal contamination gives a chance for reliable microbiological study results even in cases of bacteriuria smaller than as in the definition cited above[18].

Approximately 10-20% of patients with acute PN demonstrate positive results of blood smear[8].

## Assessment of glomerular filtration

Glomerular filtration rate (GFR) depends on the amount of functioning nephrons. GFR is a variable characterised by inter-individual differences that depends on factors including age, gender and body weight. Approximate normal GFR values are 130 ml/min/1.73m$^2$ body area for men and 120 ml/min/1.73m$^2$ body area for women[22].

Clinical relevance of GFR:

- reduction in GFR is a more sensitive index of progress of renal failure than data from urine examination, changes in electrolytes levels or fluid balance disturbances;
- GFR is a useful variable in the assessment of baseline degree of renal damage in controlled studies;
- GFR is useful in determining adjusted, reduced doses of drugs eliminated by the kidneys

Table 1 presents criteria of risk of renal damage and failure with regard to GFR and diuresis values[23]. If one functional kidney is present or if there is another abnormality of the urinary tract, assessment of GFR should be performed routinely in

**Table 1**

**Severity of renal dysfuction in relation to GRF and diuresis**

| Degree of dysfunction | Risk | Damage | Renal failure |
|---|---|---|---|
| GFR (percent of normal values) | >75% | 75-50% | <25% |
| Diuresis | <0.5 ml/kg body weight/hour for 6 hours | <0.5 ml/kg body weight/hour for 12 hours | <0.3 ml/kg body weight/hour for 24 hours nor anuria for 12 hours |

post-SIND patients once a year[24].

Determination of renal clearance, defined as plasma volume from which a marker substance can be filtered within a time unit, is the principal method of GFR evaluation. It is calculated by dividing the value corresponding to renal elimination of the marker by its plasma concentration. An ideal marker substance should, therefore, be produced in the organism at a constant rate, be eliminated exclusively by glomerular filtration, should not be subjected to metabolic reactions, synthesis, secretion of reabsorption in the renal tubules. As a substance fulfilling these criteria has not been discovered so far, for clinical purposes, GFR value is obtained using exogenous and endogenous substances which may be associated with measurement errors.

## Inulin clearance

Clearance of inulin given at constant, controlled intravenous infusion, is a reference method of GFR assessment. Inulin is a fructose polymer with molecular weight of 5200 Da, characterised by properties of an ideal renal filtration marker[25]. Because of its low solubility and necessity to heat inulin prior to administration to the patient, an analogue of inulin, called polyfructosane-S, with weight of 3500 Da, was synthesised. The classical protocol of inulin clearance measurement is troublesome and time consuming. Practically, it is better to assess clearance following single injection of inulin, however, this requires application of more advanced laboratory technology and proper interpretation.

## Urea and urea clearance

Assessment of urea level is the oldest method of GFR evaluation. Apart from changes in tubular urine flow, urea level is dependent on the rate of its production and metabolism in the organism. Urea is reabsorbed in the tubules; the reabsorption increases in dehydration and congestive heart failure. Plasma urea concentration can also be affected by protein intake, katabolic states, and intake of drugs such as tetracyclines, sulphonamides or vitamin C[10].

Clearance of urea is not a reliable measure of GFR because of its reabsorption in the kidneys. The test becomes more valuable in advanced renal failure, when urea concentration hardly depends on hydration and tubular reabsorption decreases[10,26].

## Creatinine and creatinine clearance

Creatinine is a product of metabolism of muscle proteins. It is released to the circulation at a relatively constant rate. Normally, daily variations in plasma creatinine level (Pcr) do not exceed 10%. Its concentration also depends on oral intake of meat. Creatinine undergoes free glomerular filtration, is not reabsorbed or metabolised in the kidneys, yet, it is partially secreted in the proximal segment of the renal tubules. In GFR assessment, Pcr is most frequently used, however, this method is associated with many inconveniencies[25,27,28]. Numerous formulas for GFR assessment based on Pcr have been elaborated that consider variability of creatinine level depending on age, gender, muscle mass, such as Cockroft's and Gaulter's formulas, or the MDRD formula[29,30]. These formulas do not apply in persons with altered proportions of the body, reduced muscle mass or with muscular disorders. Reduction in muscle mass is a frequent phenomenon in post-SIND patients, which limits usefulness of GFR assessment based on Pcr.

Secretion of creatinine in the proximal segment of the renal tubules increases the value of creatinine clearance by 10-20%[25]. At high Pcr, tubular secretion of creatinine increases, which results in increased GFR values in patients with moderate and severe renal failure[31]. In Pcr assessment, standard Jaffe's reaction is most often used that does not differentiate creatinine from other chromogenes not secreted in the urine, which results in lower GFR values by 10-20%[10]. In case of normal renal function, the effects of the above errors disappear, which results in creatinine clearance levels similar to that of inulin. In very early states of renal diseases, tubular secretion of creatinine can increase, which is sometimes interpreted as an increase in GFR of about 10-20 %. Trimethoprim and cimetidine also reduce tubular secretion[32]. Intake of cephalosporins can result in falsely positive result of the standard Jaffe's reaction[10].

In post-SIND patients, low sensitivity of GFR assessment using creatinine clearance was observed[3,33]. In patients with unilateral ureter occlusion, Pcr can be normal or only slightly increased because of compensatory function of the second kidney.

According to the European Best Practices Guidelines as of 2005[26], the following equation is considered to be the preferred formula for GFR assessment that is also useful in patients with significantly reduced GFR values:

GFR=(creatinine clearance + urea clearance)/2

With progressing renal failure, a linear relation between GFR fall and reverse Pcr[10] occurs.

### Methods using radioisotope markers ($^{51}$CrEDTA, $^{99m}$TcDTPA, $^{125}$Iub $^{131}$I-iothalamate and iohexol)

In many western European countries, clearance of $^{51}$Cr-EDTA ($^{51}$Cr-chelated versenate) administered in a single injection is the standard method of GFR assessment. This marker enables clearance assessment with high accuracy – differences between the measurements are lower than 1%[8]. Half-life of the marker is 1 month, which facilitates storage. Risk of exposure to radiation and high price of the marker constitute some of inconveniences of the method[27].

Iothalamate is a marker of 614 Da molecular weight that can be marked with $I^{131}$ or $I^{125}$. Iothalamate clearance shows good correlation with inulin clearance, nonetheless, in patients with low GFR values, overestimation of the result of up to 12% was observed[34]. For GFR assessment, non-marked iothalamate can also be used. This requires application of high performance liquid chromatography (HPLC) or x-ray fluorescence[35].

Clearance of $^{99m}$Tc–DTPA (Tc99m-chelated diethylene-triaminopentaacetate) administered in single injection demonstrates satisfactory correlation with $^{51}$Cr-EDTA clearance in children with reflux nephropathy, although, according to Rodman, binding of DTPA to plasma proteins may be associated with measurement errors[36]. $^{99m}$Tc–DTPA is a marker commonly used for GFR assessment by means of scintigraphy. The study is convenient, as it does not require blood drawing from the patient and is of significant clinical importance, because it provides information on renal anatomy. Intensity of collection of the marker during particular phases enables formulating conclusions about the rate of filtration separately for each kidney.

Exposure to radiation drives a search for non-isotope-labeled markers. Iohexol is a low-osmolality, non-ionised contrast marker of 821 Da molecular weight used in angiography and urography. The comound is distributed within the extracellular space and eliminated by means of glomerular filtration[37]. An algorithm for GFR assessment with an empirical formula of volume distribution following single intravenous administration of iohexol was created. The method gives reliable results in infants and older children[37].

### Cistatin C (cC)

cC is a protease inhibitor produced at a constant rate by nuclear cells. cC undergoes glomerular filtration[38]. Significantly large fraction of cC is subjected to catabolism in the proximal segment of the tubule, however, it is neither secreted nor transported back into the blood. This property is associated with the fact that cC clearance is not appropriate for GFR assessment; however, plasma concentration of the substance proves to be a valuable marker of glomerular filtration. According to the majority of researchers, cC concentration does not depend on inflammation or fever[38,39]; however Manetti suggests that cC level is dependent on the acute phase protein, CRP and functional status of the thyroid gland[40]. There are conclusions that neoplasms can cause variations in cC level[41,42], yet, many authors do not agree with this opinion[38,39]. Independence of cC level reference values of age, gender and muscle mass is an advantage of cC as a GFR marker[43]. Knight argues with this view pointing out to a tendency to higher cC concentrations in the elderly, in males and in patients with large body mass[44].

Evaluation of GFR using cC level is comparable to Cr-EDTA clearance and shows higher specificity than the measurement based on creatinine clearance, Pcr, PUrea[27,28,41,42].

### Imaging studies of the upper urinary tract

Ultrasound examination (USG) and intravenous urography have until recently been recognised as standard imaging studies of the urinary system. In the eighties, Grudny wrote that one of these studies should be performed in post-SIND patients at admission to the hospital to preliminary assess morphology of the upper urinary tract and to detect possible inborn or acquired abnormalities influencing future management approach[42]. Because of higher safety and specificity, renography – scintigraphic examination of the kidneys – is replacing urography in many applications. As a set of imaging studies used for diagnosis of urolithiasis in post-SIND persons, Biering-Sorensen recommends renography, USG of the urinary tract and plain x-ray of the abdomen[24]. Computed tomography of the abdominal cavity and urography are recommended as methods of advanced evaluation of the kidneys in cases of presence of abnormalities found in renography and USG[3].

### Plain x-ray of the abdominal cavity

It is a simple study helpful in detection of concrements containing calcium, amonium-magnesium phosphate and cystin. The study is not capable of visualising uric acid concrements or concrements that overlap over the bone structures during x-ray examination. According to Linsenmeyer[45], sensitivity of plain radiogram in diagnosis of urolithiasis in post-SIND patients is 20.97%. To more precisely localise the concrement, classical tomography is sometimes used.

### Intravenous urography

Common use of USG and renal scintigraphy resulted in a significant decrease in frequency of performance of urography. Unfavourable effects associated with urography include risk of allergic reactions following intravenous administration of the contrast medium and exposure to radiation associated with the necessity to perform a series of x-rays. However, because of a high accuracy in imaging anatomical structures, urography, especially in tomographic sequences, is very useful in imaging of widening of the pelvic-calyceal system (PCS), ureters, when renal cancer is suspected and in case of doubts in diagnosis of urolithiasis[3].

Specificity of urography is significantly higher than that of ultrasound examination. Percentage of false positive results is markedly lower for urography; the study enables precise lo-

calisation of urinary tract obstruction and allows to determine such changes as renal papillary necrosis. Urography-assisted verification of the diagnosis of urolithiasis should, according to Webb, be conducted in the following cases: presence of many concrements of irregular shape or numerous renal cysts that render detection of hydronephrosis difficult or impossible in ultrasound study or in CT scanning, impossibility of determining the level of obstruction using computed tomography[46].

## Cystography

It is a radiologic study with administration of contrast into the urinary bladder. The study is important in imaging concrements in the urinary bladder, especially those undetectable in plain x-ray as well as in imaging hypertrophic changes of vesical mucosa. Micturition cystography is an important functional study allowing to visualise vesico-ureteral reflux. It is helpful in imaging of changes located within urinary bladder mucosa. Cystographic examination is sometimes useful in recurrent infections of the urinary tract and haematuria.

## Ultrasound examination (USG)

USG is the most often used imaging study of the kidneys. Linsenmeyer recommends this examination in cases of recurrent urinary tract infection and haematuria, in cases of the lack of unequivocal evidence for presence of urolithiasis in plain x-ray of the abdomen and when renography shows abnormal results[3]. Dependence of the results on the degree of experience of the examiner constitutes an important drawback of ultrasonography[45]. Twenty-five percent of established diagnoses of urolithiasis may prove to be false positive results[46].

USG is a quick and efficacious study in the diagnosis of hydronephrosis. No correlation was found between the degree of PCS dilatation and stage of obstruction[46]. An example of a situation, where PCS dilatation does not occur, is the initial stage (first days) of acute obstruction, when, despite the rise in pressure, compliance of PCS for stretching has not yet increased. In such a case, Doppler index of vascular resistance in interlobar and arcuate arteries can be helpful[46].

## Isotope renography

It is a functional study of the structure and function of the kidneys following intravenous administration of a radioisotope marker. Apart from separate evaluation of each of the kidneys, renography enables diagnosing signs of urinary tract obstruction. Mild obstruction may be more readily detected when renography is performed after administration of a diuretic agent. Furosemide is most frequently used at a dose of 0.5 mg/kg body weight (the maximum dose is 20 mg) and given 16 minutes after infusion of the marker that – in this phase – should normally have almost completely been eliminated from the blood. The obtained images allow distinguishing dilated and patent PCSs from PCSs dilated and partially obstructed.

In many centres in highly developed countries, renography is the method of choice in initial assessment and further monitoring of renal function. The study is characterised by higher sensitivity than USG and is more objective; however, currently, there is no unequivocal evidence indicating better usefulness of USG or renography in monitoring of the upper urinary tract in patients with SIND3. According to Dillon, renography is more sensitive than urography in detection of vesico-ureteral reflux or renal scarring in the kidneys of children[47].

## Computed tomography (CT) and magnetic resonance imaging (MRI)

CT enables detection of all types of concrements in the urinary tract. Performance of USG, plain radiologic study and, for confirmation, CT allows to precisely exclude or confirm the diagnosis of urolithiasis in 90% of cases[46]. CT provides valuable information about the dimensions, location of a parenchymal structure, about signs of dilatation of the PCSs. In the majority of cases, CT allows distinguishing non-cancer renal cyst from cancer[46]. Administration of intravenous contrast enables precise imaging of the urinary tract during CT-urography. CT is sometimes considered a first-line test in urolithiasis[46].

MRI enables high-quality imaging of anatomical structures at any plane, presentation of the results in a form of 2D and 3D reconstructions. Intravenous contrast agent used in MRI study is hypo-allergenic. Frequency of use of MRI as an imaging method alternative to urography has been increasing.

## Conclusions

Contemporary complex care for post-SIND patients should include systematic monitoring of renal function both during the first hospitalisation following spinal injury and during subsequent follow-up. Detailed history and physical examination constitute the principle of effective diagnostic procedures. Availability and expected clinical relevance affect selection of additional diagnostic techniques. If possible, diagnostic approach should involve non-invasive techniques of low potential harmfulness as first-line management. In post-SIND patients, systematic, reliable, screening assessment of glomerular filtration (e.g. $^{51}$CrEDTA or $^{99m}$TcDTPA clearance or cystatin-C level assessment) is indicated as well as routine imaging of the kidneys such as renography or USG. Supplementary tests may include urography and cumputed tomography of the abdominal cavity.

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