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Kidney efficiency index quantitative parameter of a dynamic renal scintigraphy. II. usefulness in the diagnosis of obstructive nephropathy

Pawel Cichocki[1], Krzysztof Filipczak[2], Anna Plachcinska[2], Jacek Kusmierek[1]

[1]Medical University of Łódź, Department of Nuclear Medicine, Poland
[2]Medical University of Łódź, Department of Quality Control and Radiological Protection, Poland

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Abstract

BACKGROUND: One of the main indications for DRS is a diagnosis of obstructive uro-/nephropathy. In standard practice, this study includes the assessment of sequential scintigraphic images, renographic curves and such quantitative parameters as T_{MAX}, $T_{1/2}$ and split function of each kidney (SF). Due to the relative nature of SF and limitations of diagnostic capabilities of T_{MAX} and $T_{1/2}$, DRS was expanded to include new quantitative parameters describing kidney function in absolute values. This study aims to evaluate the usefulness of kidney efficiency index (KEi) — new, in-house developed parameter proportional to the average clearance function of the kidney.

MATERIAL AND METHODS: The study included 156 people aged 18–84 (average 51) years. The first group, from which normative values of new parameters were determined, consisted of 20 healthy volunteers. The second group consisted of 136 patients selected retrospectively, based on archived scintigraphic data. "Normalcy rate" (percentage of normal results among selected 62 patients with a low likelihood of obstructive uro-/nephropathy) was used to evaluate the reliability of KEi. A comparative differential analysis of obstructive uro-/nephropathy, based on standard and new DRS parameters, was performed on selected 74 patients (92 kidneys) with single functioning kidney or bilateral obstructive uropathy, where SF is unreliable.

RESULTS: Normative values: KEi $\geq$ 8; Normalcy rate for KEi: 95%. In comparison with standard DRS evaluation, application of KEi changed the diagnosis in 1/3 of assessed kidneys (from uropathy to nephropathy in 27/92 kidneys and vice versa in 4 kidneys).

CONCLUSIONS: KEi enables reproducible, quantitative assessment of absolute kidney function without any modifications of the standard DRS protocol. Its values can be compared between independent studies (e.g. follow-up examinations). KEi corrected the diagnosis of obstructive uro-/nephropathy in cases of single functioning kidney or bilateral obstructive uropathy.

KEY words: humans; kidney; radioisotope renography; radiopharmaceuticals; technetium Tc 99m-ethylenedicysteine

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Introduction

Dynamic renal scintigraphy (DRS) allows the evaluation of two functions of the kidney — uptake function and transport function. Interpretation of this study consists of visual assessment of sequential scintigraphic images, renographic curves and analysis of quantitative parameters, such as an individual contribution of each kidney to their total function (SF — split function) as well as times T_{MAX} and $T_{1/2}$ [1–3].

SF is the most important quantitative parameter in the standard DRS study and is often critical when making crucial clinical decisions (e.g. qualification of patients for nephrectomy). However, it has a significant limitation. Due to the fact that it shows the function of one kidney relative to the other, there are situations in which its value loses credibility, e.g. when assessing the function of a single kidney, or in case of disorders affecting both kidneys. Due to significant, often fundamental importance of DRS in making decisions about further management of patients, there are attempts to expand this study with additional parameters allowing

Correspondence to: Paweł Cichocki
8/10 Czechosłowacka St, 92–216 Łódź
phone: 42 675–72–90; fax: 42 675–72–85
e-mail: pawelcichocki.zmn@gmail.com

Table 1. Demographic data of all examined groups

	Number of people (number of kidneys in parentheses) and their sex					Age
	Total	Women	Men	Min.	Max.	Avg. ± SD
Group I	20 (40)	15	5	26	66	50 ± 11
Group II	136 (216)	94	42	18	84	52 ± 18
Subgroup IIA	62 (124)	48	14	18	79	48 ± 17
Subgroup IIB	74 (92)	46	28	18	84	57 ± 19

the assessment and monitoring of absolute renal function also in the above-mentioned situations.

One such option is to determine the value of glomerular filtration rate (GFR) and compare it with SF to calculate single-kidney GFR (SKGFR) [4]. However, this requires additional radioisotope studies of blood samples taken from the patient after intravenous administration of the radiopharmaceutical (^{99m}Tc-DTPA), which are not widely available. Assessment of renal function in absolute values within the DRS itself, without the need for additional tests, is made possible by calculating clearance of radiopharmaceuticals using gamma-cameras (camera-based clearance), but its determination requires extending the DRS protocol by accurate measurement of injected activity and the depth of kidneys [5, 6].

This study evaluates the diagnostic potential of a new, original parameter — Kidney Efficiency index (KEi), generated using software developed in our Department [7, 8], that allows the assessment of renal function in absolute values, but without the need for additional tests or modification of the standard DRS protocol. A model clinical problem for analyzing the usefulness of the above-mentioned parameters is the differential diagnosis of obstructive uro- and nephropathy, which is the most common indication for DRS.

Material and methods

The study covered 156 people aged 18–84 (average 51) years.

The subjects were separated into two groups. Group I — control, consisting of 20 healthy, adult volunteers (40 kidneys), which was used to determine normative values of evaluated parameters. Inclusion criteria for this group were as follows:

— no history of past or ongoing urinary tract diseases or other conditions that may lead to impaired renal function (such as systemic lupus, diabetes or uncontrolled hypertension)
— no features of urolithiasis, hydronephrosis, scarring or other focal lesions (e.g. cysts) in the kidneys in ultrasound, performed on the same day as DRS
— serum urea and creatinine levels within normal limits in tests performed on the same day as DRS

Group II included 136 adult patients, retrospectively selected from among those who underwent DRS in our Department in the years 2016–2019, based on archived medical documentation, including full data from the DRS study. In total, 216 kidneys were assessed (some patients from group IIB had only one functioning kidney). This group consisted of:

Subgroup IIA — 62 patients without scintigraphic features of obstructive uropathy or nephropathy (124 kidneys)

Subgroup IIB — 74 patients with no or trace function of one kidney (defined as SF < 10%); or with features of obstructive uropathy of both kidneys in standard study (92 kidneys in total)

Demographic data of all examined groups is summarized in Table 1.

All subjects underwent DRS performed according to the standard protocol used in our Department. All subjects drank 0.5 l of water about 30 minutes before the study and urinated just before commencing image acquisition. DRS was performed in the supine position using one of the GE scintillation cameras: Infinia Hawkeye 1, Infinia Hawkeye 4 or Optima NM/CT 640, equipped with low-energy general-purpose collimators (LEGP), after administration of standard activity of 111 MBq ^{99m}Tc-EC [9, 10]. Field of view of the detectors covered both the kidneys and the heart of the subject and the images were recorded in a 128 x 128 pixel matrix. In case of a significantly slowed down urine outflow, i.e. renographic curve remaining above 30% of the peak level for the entirety of the base study (20 min.), DRS was extended by a diuretic test, carried out in accordance with the "F+20" protocol for additional 10 minutes [11].

Routine visual assessment of 2-minute sequential scintigraphic images and renographic curves were performed in all subjects, as well as the assessment of basic quantitative parameters obtained after conventional scintigraphic data processing. In group II, kidneys with features of obstructive uropathy or nephropathy were distinguished on this basis. Kidneys meeting at least 2 of the following 3 criteria were considered nephropathic: SF < 42%, T_{MAX} > 7 min. or presence of uptake defect(s) in the peripheral part of the kidney cortex determined as a consensus by two specialists based on visual assessment of sequential images obtained in the uptake phase. On the other hand, absence of renographic curve decrease, or its decrease by less than 50% from the end of the case study after the diuretic test, were considered as features of obstructive uropathy (total or incomplete obstructive uropathy, respectively).

Afterwards, additional post-processing of scintigraphic data was performed, using the ImageJ program with the original plugin developed in our Department. The method of determining ROIs of heart, kidneys and extrarenal background was shown in the work by Filipczak et al. [7, 8]. ROIs plotted in this way were then used to generate time-activity curves showing changes of the radiopharmaceutical concentration in the heart and kidneys (the latter being corrected by subtracting non-renal background activity). These curves served as the basis for the calculation of all assessed parameters.

Based on Rutland's theory [12], uptake constant K was determined for each kidney [7, 8]. Its value is proportional to the clearance function of a kidney. Then the average value of this parameter per pixel of whole kidney ROI was calculated, to make it independent from the size of the organ, which leads to obtaining KEi.

Reliability of assessed parameters was evaluated in multiple ways. KEi values, as shown in work by Filipczak et al. [7, 8]. were strongly correlated with single-kidney eGFR (SKeGFR), where eGFR was calculated using the CKD-EPI formula [13–15] and multiplying it by SF value of each kidney.

"Normalcy rate" — the percentage of results within the normal range (according to normative values determined in the group of healthy volunteers) in group IIA, that is, in patients with no scintigraphic features of uropathy or obstructive nephropathy in standard DRS, was also used as a verification of the reliability of the method.

Next, a comparative analysis of the differentiation of obstructive uro-/nephropathy was performed based on standard and new DRS parameters in IIB subgroup, i.e. in situations where SF is unreliable.

Statistica version 13.1 was used for statistical analysis. Normality of data distributions was tested using Shapiro-Wilk's test. In group I, the distribution of KEi values was normal, while values of T_{MAX} deviated from normal distribution. In group II and each of its subgroups, values of both parameters deviated from normal distribution. The statistical significance level (p) used in the study was 0.05.

Results

Due to normal distribution of KEi values in the control group (I), its normative value was assumed as mean — 2 standard deviations, while for T_{MAX}, mean + 3 standard deviations were taken as normal limit. The results are summarized in Table 2.

KEi was within normal range in 118/124 kidneys from subgroup IIA (with very low probability of obstructive uro-/nephropathy) — "normalcy rate" 95%. The distribution of KEi values in group I and subgroup IIA was very similar (Fig. 1A and 1B, respectively).

In subgroup IIB (patients with bilateral uropathy or single active kidney), according to the standard DRS criteria assumed in this study, obstructive uropathy was found in 18/92 kidneys, and obstructive nephropathy was diagnosed in 25/92 kidneys. Distribution of KEi values in this subgroup was significantly different than in groups of healthy kidneys (Fig. 1C). Use of KEi changed the qualification in 31/92 kidneys (1/3) — in 4 cases (4%) corrected the qualification from nephropathy to uropathy, while in 27 cases (29%) KEi was below normal limit despite of lack of features of nephropathy in the evaluation of standard scintigraphic parameters (Fig. 2).

Table 2. Values of assessed parameters in examined groups with assumed normative limits

	TMAX [min]	KEi
Group I	3,6 ± 1,1	12,78 ± 2,46
Normal limits	< 7	≥ 8
Group II		
Subgroup IIA	4,4 ± 2,2	12,20 ± 2,87
Subgroup IIB	13,8 ± 11,3	9,32 ± 5,45

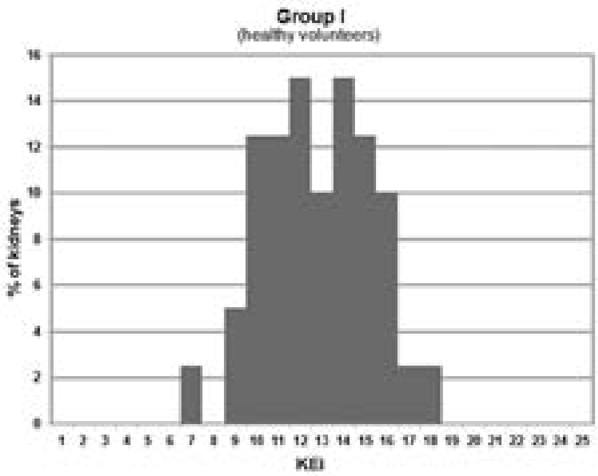

Figure 1A. Distribution of KEi values in kidneys from group I

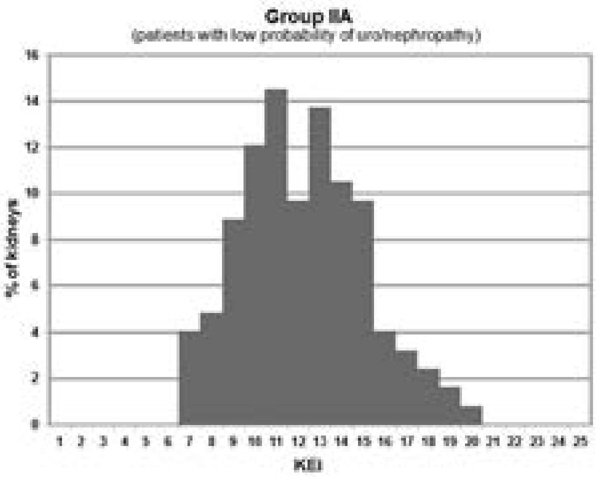

Figure 1B. Distribution of KEi values in kidneys from subgroup IIA

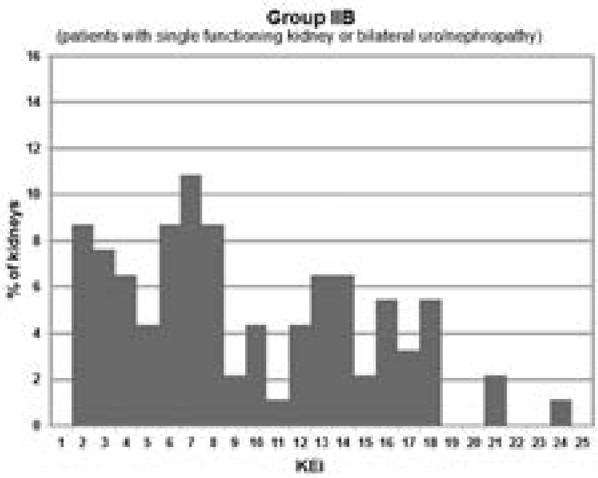

Figure 1C. Distribution of KEi values in kidneys from subgroup IIB

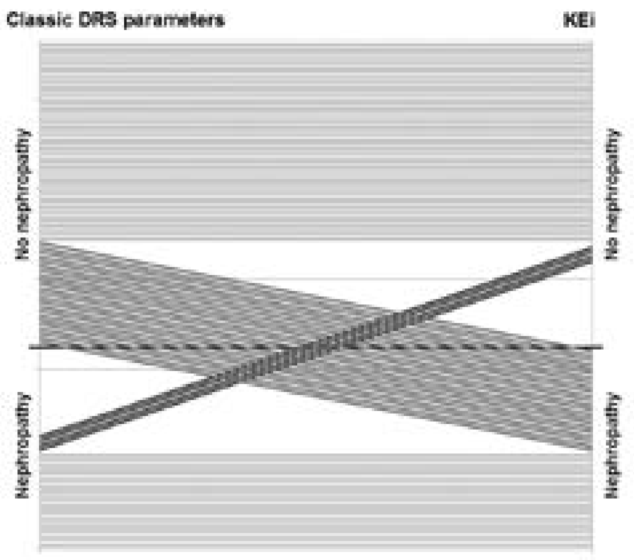

Figure 2. Change of kidney qualification in group IIB based on the values of KEi

There were 3 patients qualified as bilateral uropathy, whose kidneys had SF well within normal ranges and displayed no significant uptake defects, while KEi showed features of bilateral nephropathy. In the group of patients with single functioning kidney, in 7 cases KEi changed the classification to nephropathy while all 3 standard criteria suggested normal function of the kidney, that is SF was between 90 and 100%, T_{MAX} between 3 and 6 min. and visual assessment revealed no uptake defects at all.

Discussion

SF, which is the main quantitative parameter of DRS, due to its relative nature has significant limitations reducing its usefulness in certain clinical situations. In case of bilateral renal dysfunction or only a single functioning kidney, reliable assessment of renal function is only possible by supplementing SF with the value of GFR of a given patient. However, this requires performing additional studies, e.g. using accurate, but time-consuming and labor-intensive methods for determining glomerular filtration with radioisotopes (^{99m}Tc-DTPA clearance) or as a simpler, but less accurate method for calculating estimated GFR using biochemical studies (e.g. serum creatinine level).

Therefore, methods that allow an assessment of renal cortex function in absolute values are being developed, based only on scintigraphic data obtained with gamma-cameras in DRS, without the need for taking blood samples or urine collection. Several such protocols have been created and camera-based clearance methods are even an integral part of modern scintillation camera software. However, for these techniques acquisition of additional - non-standard data is necessary, as described in the work by Filipczak et al. [7, 8], which in turn requires modification and expansion of the standard DRS protocol.

Original parameter KEi does not have these disadvantages. It is relatively easy to determine and relies only on post-processing of standard scintigraphic data. Hence it can be used both routinely, or only in cases in which assessment of classic DRS parameters does not provide a conclusive diagnosis. It can also be applied retrospectively with ease, for example for scientific purposes.

One of the important arguments supporting the usefulness of this parameter, apart from its strong correlation with SKeGFR shown in work by Filipczak et al. [7, 8], is its high normalcy rate. In a group of patients with a very low probability of uropathy or nephropathy according to the standard DRS evaluation — subgroup IIA, KEi also showed values within the normal range in 95% of cases and the distribution of its values was very similar to group I. This confirms the accuracy of the normative limit established on a selected group of healthy volunteers. Distribution of KEi values in subgroup IIB, which consisted of both normally functioning and nephropathic kidneys, was significantly different.

Value of KEi, that represents the average clearance function of a kidney, is completely independent of its size. This allows determination of normative values, based on a group of healthy volunteers with no impairments of kidney function, that can later be used for evaluation of other kidneys, regardless of their size. This parameter can be useful not only in the diagnosis of obstructive nephropathy, but also for the differentiation of a small, but normally functioning (hypoplastic) kidney from an insufficient one (e.g. cirrhotic), and in assessing a small kidney in the diagnosis of renovascular hypertension. This will be the subject of our further research.

In summary, it should be noted that KEi extends the capabilities of DRS with a repeatable, quantitative assessment of absolute, individual kidney function. This parameter does not require any modifications of a routine protocol of the study (and thus can be determined in post-processing, e.g. only if the standard DRS result is ambiguous). It was shown that use of this parameter improves the diagnostic effectiveness of DRS in the differential diagnosis of obstructive uropathy and nephropathy.

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