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ORIGINAL ARTICLE

Comparison of ^{99m}Tc-DTPA and ^{51}Cr-EDTA for glomerular filtration rate measurement with the continuous infusion method

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Abstract

Background In late 2018, the production of ^{51}Chromium-labelled ethylenediamine tetra-acetic acid (^{51}Cr-EDTA), a validated and widely used radio-isotopic tracer for measuring glomerular filtration rate, was halted. Technetium-99m-diethylenetriaminepentaacetic acid (^{99m}Tc-DTPA) has been validated for GFR measurement with a single bolus injection, a procedure not suitable in patients with extracellular compartment hyperhydration. In such cases, a bolus followed by continuous infusion of the tracer is required. The aim of this study was to evaluate whether ^{99m}Tc-DTPA with the infusion protocol can replace ^{51}Cr-EDTA for GFR measurement.

Methods We conducted a prospective single centre study during February and March 2019. All patients referred for GFR measurement received both radiotracers simultaneously: ^{51}Cr-EDTA and ^{99m}Tc-DTPA bolus and continuous infusion were administered concomitantly through the same intravenous route. Over four and a half hours, plasma and urine samples were collected to calculate urinary and plasma clearance.

Results Twenty-two patients were included (mean age 63.4 ± 17.5 years; 68% men). Mean urinary clearance of ^{51}Cr-EDTA and ^{99m}Tc-DTPA was 52.4 ± 22.5 mL/min and 52.8 ± 22.6 mL/min, respectively ($p = 0.47$), with a mean bias of 0.39 ± 2.50 mL/min, an accuracy within 10% of 100% (95% CI 100; 100) and a Pearson correlation coefficient of 0.994. Mean plasma clearance of ^{51}Cr-EDTA and ^{99m}Tc-DTPA was 54.8 ± 20.9 mL/min and 54.4 ± 20.9 mL/min, respectively ($p = 0.61$), with a mean bias of − 0.43 ± 3.89 mL/min, an accuracy within 10% of 77% (95% CI 59; 91) and a Pearson correlation coefficient of 0.983.

Conclusions Urinary and plasma clearance of ^{99m}Tc-DTPA can be used with the infusion protocol to measure GFR.

Clara Balouzet and Arthur Michon-Colin contributed equally to this work.

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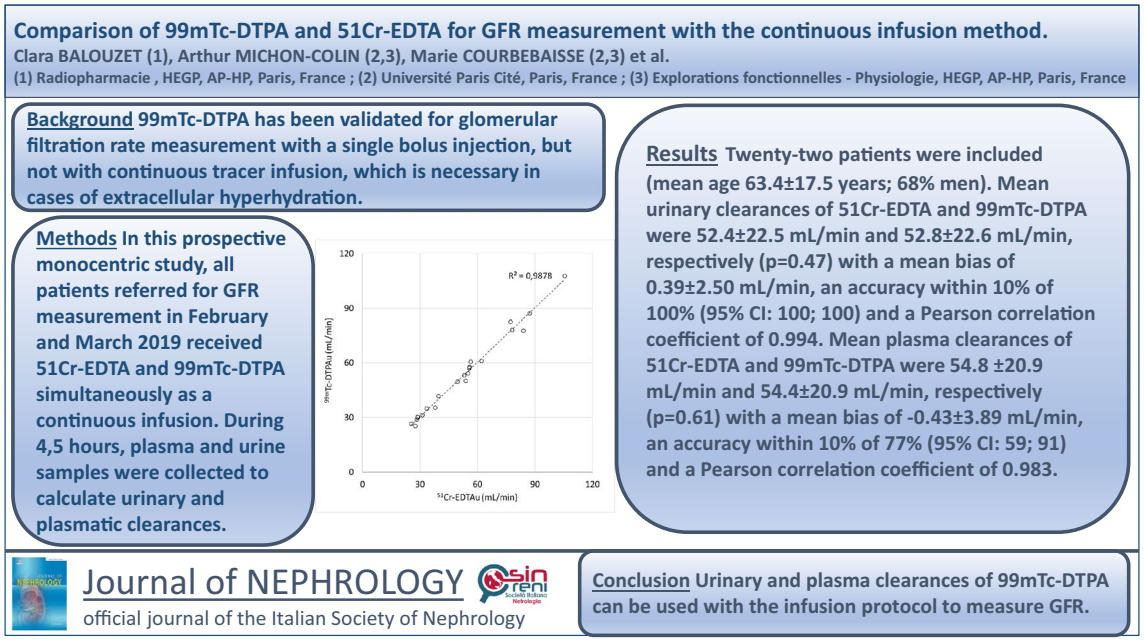
Graphical abstract



Keywords Glomerular filtration rate · ^{99m}Tc-DTPA · ^{51}Cr-EDTA · Infusion protocol

Introduction

Glomerular filtration rate (GFR) is commonly estimated with formulas based on blood creatinine concentration, such as Modification of Diet in Renal Disease (MDRD) or Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) [1, 2]. These methods are, however, too imprecise in many clinical situations which require a direct measurement of GFR with the injection of an exogenous tracer [3–5]. Urinary clearance of inulin is the gold standard for GFR measurement [4], but inulin was recently withdrawn from the market in France and several other countries for safety reasons [6, 7]. ^{51}Chromium-labelled ethylenediamine tetra-acetic acid (^{51}Cr-EDTA) has been widely used and validated against inulin as a radio-isotopic tracer for GFR measurement in Europe [8–11].

Unfortunately, the production of ^{51}Cr-EDTA was halted for financial reasons at the end of 2018, compelling nephrologists and radio-pharmacists to urgently consider an alternative radio-isotopic method, both for initial GFR measurements and for longitudinal follow-up of patients.

Diethylenetriaminepentaacetic acid (DTPA) is very similar to EDTA and can be labelled with technetium-99 m (^{99m}Tc-DTPA) [12]. ^{99m}Tc-DTPA is mostly used for the assessment of split renal function by scintigraphy. In a French multicentre study, we recently validated the use of ^{99m}Tc-DTPA for GFR measurement after a single bolus against ^{51}Cr-EDTA that was still available at that time [13]. Of note, one difficulty in the use of ^{99m}Tc-DTPA is the much shorter half-life of ^{99m}Tc compared to that of ^{51}Cr (6 h vs 28 days), thus requiring the use of a correction factor of the radioactivity measurement considering the radioactive decay.

Importantly, in case of defective urine collection, which is a frequent and unpredictable issue during GFR measurement (that requires several timed urine samplings), it is not possible to use urinary clearance and we must consequently use plasma clearance. Measurement of the plasma clearance of a tracer after a single injection is based on the Bröchner-Mortensen equation, conceptualized in a bicompartmental model to predict the distribution of the tracer [14]. This model is no longer valid in case of extracellular expansion, as the distribution from plasma to extracellular fluid is distended leading to an overestimation of the GFR [5]. However, it is still possible to interpret plasma clearance using a bolus injection followed by continuous perfusion of a radiotracer in case of extracellular volume expansion, as we previously did with ^{51}Cr-EDTA [15, 16], because it requires reaching a steady state, regardless of the volume of distribution of the tracer. The summary of the differences between these two measurement methods is presented in Table 1. Consequently, in clinical practice, to be able to give a reliable measurement of GFR for patients with extracellular volume expansion, we must therefore use a continuous

Table 1 Differences between the two GFR measurement methods

	Single bolus injection method	Continuous infusion method
Advantages	–Single venous route –Usable with all the available reference tracers*	**–Plasma clearance reliable in case of ECI**
Disadvantages	**–Plasma clearance not reliable in case of ECI**	–Two venous routes –Not available with Iohexol/Iothalamate

ECI extracellular compartment hyperhydration

*^{51}Cr-EDTA, ^{99m}Tc-DTPA, Iohexol, Iothalamate

infusion method. Of note, such cases are frequent because many patients requiring GFR measurement, including patients with chronic kidney disease (CKD), advanced congestive cardiac failure or ascites, have extracellular volume expansion and often encounter difficulties to completely void their bladder. Access to a GFR measurement method using continuous perfusion of a radiotracer is therefore essential in all centres previously using ^{51}Cr-EDTA. This method has not yet been validated with ^{99m}Tc-DTPA.

In the present work, we compared the performance of ^{51}Cr-EDTA, just before the announced definitive withdrawal of this reference radiotracer, and ^{99m}Tc-DTPA for GFR measurement using a continuous infusion method.

Methods

Study design and participants

We conducted a prospective single centre study: all adult (age > 18 years) patients referred to our centre for GFR measurement in February and March 2019 were asked to participate, regardless of their estimated extracellular volume. Pregnancy and breastfeeding were exclusion criteria. Past medical history, treatment and anthropometric data were recorded. Extracellular compartment hyperhydration was clinically defined by the presence of oedema and/or ascites on the day of the GFR measurement. Patients with CKD were classified according to the commonly used KDIGO guidelines [17].

This study was classified as non-interventional by the DRCI (Délégation à la Recherche Clinique et à l'Innovation) of APHP (Assistance Publique–Hôpitaux de Paris). All patients received oral and written information about the study before inclusion, and signed informed consent. The study was approved by our local Ethics Committee (CER-APHP.5, IRB registration #00011928), and for scientific use, all data were anonymized. Research was conducted in accordance with good clinical practices and the Declaration of Helsinki.

Description of GFR measurements

^{51}Cr-EDTA 3.7 MBq/mL solution for injection (GE Healthcare, France) and Technescan DTPA™ (Curium, France) radiolabelled with sodium pertechnetate (^{99m}Tc) eluate from Tekcis® generator (Curium, France) to obtain ^{99m}Tc-DTPA were the two tested radiotracers in this study. ^{51}Cr-EDTA, which was still active and available in our unit at the time this study was conducted, was used as the reference tracer.

Injections started in the morning between 09:00 and 10:00 a.m. Fasting was not required. One bolus of each radiotracer was first administered. Then two continuous Y infusions (in order to use a single intravenous route) were concomitantly administered at a rate of 1.5 mL/min for 4 h. This simultaneous administration does not interfere with the accuracy of radiotracer determinations, due to the difference in energy of their gamma radiation. Moreover, the concomitant infusion of the two radiotracers using a Y infusion allows both tracers to be injected under the same conditions and to start clearance calculations at the same time. Administered doses were determined with calculations based on patients' weight, body surface area and estimated GFR (using the MDRD equation [1]) (Table 2). A sample of the continuous infusion solution and a sample of the bolus syringe were taken and syringes were weighed before and after injection in order to calculate the precise injected amount of the radiotracer (necessary to calculate the infusion rate of radioactivity, using the flow rate of the infusion pump, which is fixed and known). Over four and a half hours, plasma and urine samples were collected to

Table 2 Doses of radiotracer calculations

	Calculated dose (MBq)
Bolus	$\frac{\text{weight(kg)}}{2} \times \frac{3.7}{100}$
Infusion	$0.75 \times \frac{\text{eGFRMDRD}(\text{mL/min/1.73m}^2)}{1.73} \times \text{BSA}(\text{m}^2) \times \frac{3.7}{100}$

BSA body surface area, *eGFR MDRD* estimated glomerular filtration rate by Modification of Diet in Renal Disease equation, *MBq* megabecquerel

calculate urinary and plasma clearance as follows: after a 60 min resting period to allow the plasma concentrations of the radiotracers to reach equilibrium, urine was collected every 30 min for 8 consecutive periods and 7 blood samples were collected from the contralateral arm to the injection every 30 min, at the mid point of each urine collection period. Completion of each urine collection was checked using urine creatinine rate. One urine and plasma sample each was collected before injections in order to determine the radioactivity background in each sample matrix.

Radioactivity of urinary, plasma and syringe samples were measured with the Cobra II® 5003 (Packard®) well gamma counter. Each sample was counted for 4 min in the appropriate energy window: 140–160 keV and 240–400 keV for ^{99m}Tc and ^{51}Cr, respectively. ^{99m}Tc radioactive decay was corrected depending on when the radioactivity of each sample was counted.

Urinary clearance was calculated for each radiotracer as the average of seven clearance measurements, defined as urine activity multiplied by urine output, divided by plasma activity. Plasma clearance was calculated by dividing the rate of infused activity by the mean plasma activity at steady-state. Indeed, once the steady state is reached (i.e. stable plasma activity of the radiotracer), the infused radioactivity rate is equal to the GFR multiplied by this steady-state plasma radioactivity, according to the principle of "entries equal to outflows" [18, 19]. As intra individual measurements were compared, GFR values were not corrected for body surface area.

Statistical analysis

Measured GFR of both radiotracers were compared using paired *t* tests. Precision and accuracy of GFR of ^{99m}Tc-DTPA, compared with reference ^{51}Cr-EDTA, were evaluated using bias (difference between values obtained by both radiotracers), relative bias (bias divided by value obtained using ^{51}Cr-EDTA, expressed in percentage), intrinsic precision (absolute difference between individual bias and mean bias, divided by reference value, expressed in percentage), Pearson correlation coefficients, accuracy within 5, 10 and 30% (AW5, AW10 and AW30, percentage of ^{99m}Tc-DTPA-derived values within 5, 10 or 30% of ^{51}Cr-EDTA-derived values, respectively), and root mean square logarithmic error (RMSLE, calculated from the difference of the logarithmic estimated and reference values). The 95% confidence intervals (CIs) for AW5, AW10, AW30 and RMSLE were calculated using 1,000 bootstrap iterations. Performance of both radiotracers was also compared graphically using linear correlation and Bland–Altman plots [20]. All tests were two-sided using a significance level of 0.05.

Results

Patients

A total of 22 patients were included in the study. Characteristics of the patients are reported in Table 3. Mean age was 63.4 ± 17.5 years, 68.2% were males and mean body mass index was 26.4 ± 4.9 kg/m^2. Mean estimated GFR (using the creatinine-derived CKD-EPI equation [2]) was 55.8 ± 21.7 mL/min. Urine collection was complete (7 samples) for 17 of 22 patients, with an average of 6.5 urine collections per patient. Eleven patients had CKD: 1 (9.1%), 3 (27.3%), 1 (9.1%), 3 (27.3%) and 3 (27.3%) in stage 1, 2, 3a, 3b and 4, respectively. Patients were classified into two groups based on whether or not clinical extracellular volume expansion was present (Table 3).

GFR measurements

Linear correlations and Bland–Altman plots for urinary and plasma clearance of both radiotracers are shown in Fig. 1.

Mean urinary clearance of ^{51}Cr-EDTA and ^{99m}Tc-DTPA was 52.4 ± 22.5 and 52.8 ± 22.6 mL/min, respectively, with a mean bias of 0.39 ± 2.50 mL/min, a mean intrinsic precision of 3.56 ± 2.77%, a Pearson's correlation coefficient of 0.994, an AW5 of 64% (95%CI 41;77) and an AW10 and AW30 of 100% (Tables 4 and 5). Sub-group analyses showed no difference for mean urinary clearance for patients with or without extracellular compartment hyperhydration ($p > 0.05$) (Table 4).

Mean plasma clearance of ^{51}Cr-EDTA and ^{99m}Tc-DTPA was 54.8 ± 20.9 and 54.4 ± 20.9 mL/min, respectively, with a mean bias of − 0.43 ± 3.89 mL/min, a mean intrinsic precision of 6.24 ± 5.00%, a Pearson's correlation coefficient of 0.983, an AW5 of 36% (95%CI 14;59), an AW10 of 77% (95%CI 59;91) and AW30 of 100% (Tables 4 and 5). Sub-group analyses showed no difference for mean plasma clearance for patients with or without extracellular compartment hyperhydration ($p > 0.05$) (Table 4).

Mean difference between urinary and plasma clearance was 2.38 ± 10.29 mL/min for ^{51}Cr-EDTA and 1.56 ± 9.97 mL/min for ^{99m}Tc-DTPA ($p = 0.278$). For patients with extracellular compartment hyperhydration, difference was 4.05 ± 8.83 mL/min for ^{51}Cr-EDTA and 2.99 ± 9.19 mL/min for ^{99m}Tc-DTPA ($p = 0.321$). For patients without extracellular compartment hyperhydration, difference was 0.39 ± 12.00 mL/min for ^{51}Cr-EDTA and − 0.16 ± 11.07 mL/min for ^{99m}Tc-DTPA ($p = 0.641$).

Table 3 Characteristics of the study population

	Overall $N=22$	Patients with ECI $N=12$	Patients without ECI $N=10$
Demographic and clinical characteristics			
Age (years)	63.4 ± 17.5	69.6 ± 16.1	55.9 ± 16.9
Males	15 (68.2%)	8 (66.7%)	7 (70.0%)
Body mass Index (kg/m^2)	26.4 ± 4.9	26.8 ± 5.3	25.9 ± 4.7
Systolic blood pressure (mm Hg)	133 ± 12	133 ± 12	132 ± 13
Diastolic blood pressure (mm Hg)	75 ± 9	72 ± 8	78 ± 9
Heart rate (beats/min)	69 ± 12	66 ± 13	73 ± 11
Medical history			
History of diabetes	7 (31.8%)	5 (41.7%)	2 (20.0%)
History of hypertension	16 (72.7%)	8 (66.7%)	8 (80.0%)
Biological parameters			
Creatinine (µmol/L)	127.4 ± 53.6	146.2 ± 62.4	104.8 ± 30.3
eGFR CKD-EPI (mL/min/1,73m^2)	55.8 ± 21.7	45.4 ± 17.5	68.3 ± 20.1
Protein to creatinine ratio (mg/mmol)	21.6 [9.3;43.8]	33.6 [16.9;103.3]	13.9 [6.6;22.0]
Indication for referral			
Follow-up of chronic kidney disease	11 (50.0%)	8 (66.7%)	3 (30.0%)
Kidney transplant recipient	6 (27.3%)	2 (16.7%)	4 (40.0%)
Chronic elevation of serum creatinine	2 (9.1%)	1 (8.3%)	1 (10.0%)
Drug nephrotoxicity*	2 (9.1%)	–	2 (20.0%)
Heart pre-transplant check-up	1 (4.5%)	1 (8.3%)	–

Data are expressed as mean ± SD, *n* (%) or median [25th;75th percentiles]

ECI extracellular compartment hyperhydration; *eGFR CKD-EPI* estimated glomerular filtration rate using chronic kidney disease—epidemiology collaboration equation

*Corresponds to the estimation of the baseline renal function before a nephrotoxic treatment, e.g. chemotherapy, especially for the calculation of the dose to be administered

Discussion

Our prospective comparative study showed excellent GFR measurement accuracy and precision for both urinary and plasma clearance methods using infusion protocol with ^{99m}Tc-DTPA, compared to ^{51}Cr-EDTA.

As expected, the plasma clearance value was slightly higher than the urinary clearance value, reflecting the extra-renal clearance of the radiotracers. This difference was similar for both radiotracers (approximately 2 mL/min), confirming similar extra-renal handling of ^{51}Cr-EDTA and ^{99m}Tc-DTPA. Note that a standard deviation of 10% of the measured clearance is considered acceptable in our centre. This margin of error of 2 mL/min can therefore be considered acceptable up to 20 mL/min of clearance. Furthermore, this same 2 mL/min error, even if proportionately larger, will generally not have clinical consequences for patients with very low GFR. It is also important to underline that, for each GFR measurement, we performed 6 to 7 urine and blood samplings in order to be able to calculate at least 6 urine clearance measurements of the reference tracer. This repetition of measures is necessary to give the result with high precision, but necessarily implies a standard deviation. Note that GFR measurements using a single point (i.e. plasma clearance of iohexol after a single injection and with a unique plasma sample) do not have standard deviation but are less precise.

We show excellent agreement between the GFR measurement based on urinary or plasma clearance obtained with ^{51}Cr-EDTA and those obtained with ^{99m}Tc-DTPA, despite the much shorter half-life of ^{99m}Tc compared to that of ^{51}Cr, proving that the ^{99m}Tc radioactive decay correction enables GFR measurement. Of note, this result allows comparison of 2 successive GFR measurements, even if the first was made with ^{51}Cr-EDTA and the second with ^{99m}Tc-DTPA.

A few previous studies compared both radiotracers for GFR measurement based on a single bolus injection. In 1984, Rehling et al. showed no significant difference in plasma and urinary clearance between ^{99m}Tc-DTPA and ^{51}Cr-EDTA in 20 patients with variable renal function [21]. Several recent studies have confirmed this result. Andersen et al. showed no clinically relevant difference in plasma clearance between ^{99m}Tc-DTPA and ^{51}Cr-EDTA (mean bias of 1.4 mL/min) in 56 patients [22]. Simonsen et al. did not show a significant difference in mean values of GFR measured with ^{99m}Tc-DTPA or ^{51}Cr-EDTA [23].

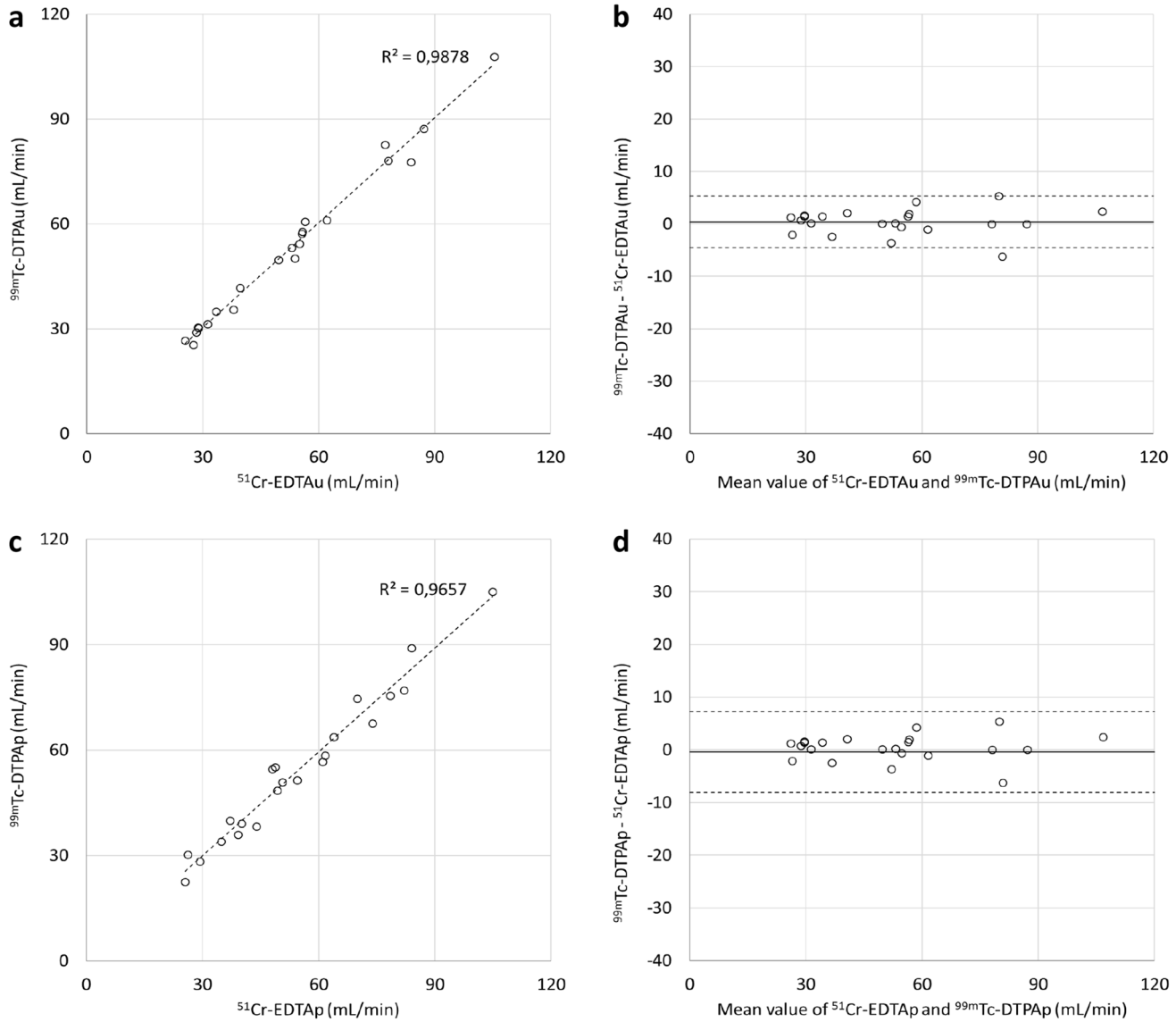


Fig. 1 Graphical comparison of clearance values measured with ^{99m}Tc-DTPA *versus* those measured with ^{51}Cr-EDTA for urinary clearance (top panels, **a** and **b**) and plasma clearance (bottom panels, **c** and **d**). Left panels (**a** and **c**) represent linear correlation between metrics obtained by ^{99m}Tc-DTPA versus those obtained with ^{51}Cr-EDTA; the dotted lines represent identity line. Right panels (**b** and **d**) represent Bland–Altman plots (values obtained with ^{99m}Tc-DTPA minus that obtained with ^{51}Cr-EDTA in function of average value obtained with both tracers); the full line represents mean bias while the dotted lines represent bias ± 1.96 × standard deviation. *^{51}Cr-EDTA* ^{51}Chromium-labelled ethylene-diamine-tetra-acetic acid, *^{51}Cr-EDTAp* plasma clearance of ^{51}Cr-EDTA, *^{51}Cr-EDTAu* urinary clearance of ^{51}Cr-EDTA, *^{99m}Tc-DTPA* Technetium-99m-diethylenetriamine-pentaacetic acid, *^{99m}Tc-DTPAp* plasma clearance of ^{99m}Tc-DTPA, *^{99m}Tc-DTPAu* urinary clearance of ^{99m}Tc-DTPA

Moralidis et al. showed good agreement between ^{99m}Tc-DTPA and ^{51}Cr-EDTA plasma clearance (mean bias of 0.0 mL/min, AW30 of 95%). However, urinary clearance was not measured in these 3 studies. A recent French multicentre study (including our centre) also showed excellent accuracy and precision of GFR measurement using ^{99m}Tc-DTPA for both urinary and plasma clearance methods, compared with ^{51}Cr-EDTA, despite an approximate 2 mL/min overestimation (accuracy within 10% of 95% for the urinary clearance and 91% for the plasma clearance) [13]. However, to the best of our knowledge, the performance of ^{99m}Tc-DTPA (compared with ^{51}Cr-EDTA) using the continuous infusion method has never been reported. Our study therefore fills this gap in the scientific literature.

Our study helps define the central role of ^{99m}Tc-DTPA, which is one of the few remaining reliable tracers for GFR measurement since ^{51}Cr-EDTA and inulin are no longer available. Of note, iohexol is widely used with the plasma

Table 4 Values of GFR measured using urinary and plasma clearance of ^{51}Cr-EDTA and of ^{99m}Tc-DTPA

	Urinary clearance (mL/min)			Plasma clearance (mL/min)		
	^{51}Cr-EDTA	^{99m}Tc-DTPA	*P* value	^{51}Cr-EDTA	^{99m}Tc-DTPA	*P* value
Overall ($N=22$)	52.4 ± 22.5	52.8 ± 22.6	0.473	54.8 ± 20.9	54.4 ± 20.9	0.606
Patients with ECI ($n=12$)	40.5 ± 18.1	40.6 ± 17.9	0.698	44.5 ± 17.1	43.6 ± 17.5	0.360
Patients without ECI ($n=10$)	66.8 ± 19.1	67.5 ± 19.2	0.558	67.2 ± 18.7	67.3 ± 18.0	0.932

Data are expressed as mean ± SD

^{51}*Cr-EDTA* ^{51}chromium-labelled ethylenediamine tetra-acetic acid, ^{99m}*Tc-DTPA* technetium-99m-diethylenetriaminepentaacetic acid, *ECI* extracellular compartment hyperhydration. *GFR* glomerular filtration rate

Table 5 Precision and accuracy of ^{99m}Tc-DTPA urinary and plasma clearance compared to ^{51}Cr-EDTA urinary and plasma clearance

	Urinary clearance	*p* value	Plasma clearance	*p* value
Mean bias (mL/min)	0.39 ± 2.50	0.473*	− 0.43 ± 3.89	0.606*
Relative bias (%)	0.95 ± 4.61	0.347*	− 0.63 ± 8.07	0.717*
Pearson correlation coefficient	0.994	–	0.983	–
Intrinsic precision (%)	3.56 ± 2.77	–	6.24 ± 5.00	–
AW5 (%)	64 [41;77]	–	36 [14;59]	–
AW10 (%)	100 [100;100]	–	77 [59;91]	–
AW30 (%)	100 [100;100]	–	100 [100;100]	–
RMSLE	0.046 [0.035;0.056]	–	0.078 [0.055;0.095]	–

Data are expressed as mean ± SD or value [95% CI]

95% CIs were determined by 1000 bootstrap iterations

^{51}*Cr-EDTA* ^{51}chromium-labelled ethylene-diamine-tetra-acetic acid, ^{99m}*Tc-DTPA* technetium-99m-diethylenetriaminepentaacetic acid, *AW5/10/30* accuracy within 5/10/30%; *RMSLE* root mean square logarithmic error

**p* value versus null

clearance method after a single injection that does not enable GFR measurement in case of extracellular volume expansion [24, 25]. Moreover, some patients may be allergic to iodinated contrast agents and iohexol cannot be used in these patients. In practice, ^{99m}Tc-DTPA (available worldwide) is the only remaining tracer allowing a valid measurement of both urinary and plasma clearance, by the continuous infusion technique, in countries where inulin has been withdrawn. Access to a continuous infusion measurement technique is mandatory, since patients with CKD often present with numerous comorbidities leading to extracellular volume expansion (making plasma clearance evaluation with a single injection unreliable) and difficulty in performing multiple urine collections (not allowing the calculation of urine clearance).

This study has many strengths. First, the prospective design of the study allows us to have no missing data, and strengthens the reliability of our results. This is also the first time that ^{51}Cr-EDTA and ^{99m}Tc-DTPA are compared during continuous perfusion. Because all patients received both tracers, they are their own controls for the comparison of ^{99m}Tc-DTPA and ^{51}Cr-EDTA, thus avoiding potential confounding factors. In addition, the continuous infusion technique has long been used routinely in our department, which prevents the occurrence of technical errors. Finally, as ^{51}Cr-EDTA is no longer available, it was urgent to validate alternatives so as not to compromise the GFR measurement of patients who would benefit from it. The demonstration of very similar values obtained with ^{99m}Tc-DTPA and ^{51}Cr-EDTA is therefore of major clinical interest.

The main limitation of our study is the limited number of included patients, but it is due to the short overlap between implementation of ^{99m}Tc-DTPA-based GFR measurement and the disruption of ^{51}Cr-EDTA. However, the robustness of our results seems sufficient despite the small number of patients, especially because of the high precision of our measurements. The rather limited range of GFRs in the included patients can also be noted. In addition, our assessment of the extracellular compartment would have been more accurate using impedancemetry. However, the clinical assessment is consistent with our current practice, and we do not use any other method for extracellular compartment assessment prior to GFR measurement.

In conclusion, this study shows that ^{99m}Tc-DTPA is a reliable alternative to ^{51}Cr-EDTA for GFR measurement, based on urinary or plasma clearance measurement, using a continuous infusion for patients with or without extracellular compartment hyperhydration.

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Data availability The data supporting the findings of this study may be shared by the authors upon reasonable request.

Declarations

Conflict of interest The results presented in this paper have not been published previously in whole or part except in abstract format. The authors have conflict of interest to declare related to this study. Dr. Balouzet reports non-financial support from Curium, outside the submitted work, Pr. Courbebaisse reports grants from Biohealth (Italy), and Advicenne (France), and personal fees from Alnylam (France), outside the submitted work.

Ethical approval This study was classified as non-interventional by the DRCI (Délégation à la Recherche Clinique et à l'Innovation) of APHP (Assistance Publique—Hôpitaux de Paris).

Human and animal rights The study was approved by our local Ethics Committee (CERAPHP.5, IRB registration #00011928), and for scientific use, all data were anonymized. Research was conducted in accordance with good clinical practices and the Declaration of Helsinki.

Informed consent All patients received oral and written information about the study before inclusion, and signed informed consent.

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