Measurement of Renal Function (GFR and ERPF)

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1. Introduction

The primary renal function is the glomerular filtration rate which correlates to the renal plasma flow via the filtration fraction. Inulin clearance has traditionally been the gold standard for the GFR and para-aminohippuric acid clearance for the ERPF. The advantage of the radionuclide method is that the cumbersome chemical determination of the aforementioned substances can be dispensed with.

If a radiopharmaceutical with properties as described above is not metabolised and is almost exclusively excreted by the kidneys, then, during a constant infusion of the radiopharmaceutical, clearance can be accurately determined from the infused volume and the plasma levels measured at regular intervals. That is provided the plasma levels have reached a steady state, whereby the quantity of infused pharmaceutical is equal to the quantity of renally excreted pharmaceutical. Urine collection, which is often inaccurate, is then unnecessary.

There are several possible radiopharmaceuticals, each with their pros and cons. An important criterion is whether any metabolism or extra-renal clearance is taking place; these are factors which cause the GFR or ERPF to be overestimated if the constant infusion method is being used.

In this protocol, the GFR and ERPF are simultaneously determined by the constant infusion method of Donker et al. 1977.

2. Methodology

This guideline is based on available scientific literature on the subject, the previous guideline (Aanbevelingen Nucleaire Geneeskunde 2007), international guidelines from EANM and/or SNMMI if available and applicable to the Dutch situation.

3. Indications

Whenever an accurate absolute measure of GFR, ERPF or FF is desired, for example when studying the influence of medicines on renal function.

4. Relation to other diagnostic procedures

There are numerous ways of estimating renal function from very simple to elaborate, with ditto precision. In every day clinical use an estimation of renal function is used on the basis of the creatinine plasma levels corrected for sex, age and race (MDRD formula). The method described here is one of the most precise measurements of renal function based on a constant infusion method with a radioactive tracer for GFR and ERPF measurement.

5. Medical information necessary for planning

a. The estimated renal function (serum creatinine, creatinine clearance).
b. The body weight and height (body surface).

c. Nature of the kidney disease.
d. Medications used (especially pharmaceuticals influencing renal function).

6. Radiopharmaceutical

Tracer:	^{125}I-Iothalamate (IOT) for the GFR ^{131}I-Sodium-iodohippurate (IOH) for the ERPF
Nuclide:	Iodine-125 Iodine-131
Activity:	the infusion consists of 100 ml physiological saline with 2,0 MBq of ^{131}I-IOH and 1,5 MBq of ^{125}I-IOT. The loading dose (priming dose) is 0,375 ml of this solution per kg of body weight supplemented by an additional 0,3 MBq of ^{125}I-IOT; the remainder is infused. If serum creatinine is below 100 µmol/l, the infusion rate is 12 ml/h; if it is between 100 to 200 µmol/l: 9 ml/h and if it is greater than 200 µmol/l: 6 ml/h. The total duration of the infusion is 5,5 h
Administration:	intravenous

7. Radiation safety

Total radiation exposure for the combined measurement of GFR and ERPF is less than 0,2 mSv. Breast feeding should be interrupted for 12 h when using hippurate according to ICRP 106, this seems also advisable for Iothalamate.

8. Patient preparation/essentials for procedure

a. The patient may have a light breakfast, but may not eat, smoke or drink coffee during the investigation
b. The thyroid should be blocked.
c. If possible, diuretics should be stopped at least 2 days before the investigation.

9. Acquisition and processing

Requirements for carrying out the investigation

a. Comfortable chair (half-seated) or bed.
b. Infusion pump.
c. Urine receptacle.
d. Precautionary IV line supplies.
e. Heparin tubes.
f. Urine pots.
g. Clock.

Procedure

a. In order to obtain sufficient diuresis during the investigation, the patient is given 200 to 250 ml of water per hour. A blank plasma sample is taken. Then, the priming dose is administered intravenously and the constant infusion is started.
b. From the arm which is contralateral to the infusion arm, 6 ml blood (heparin tube) is taken at t=90, 150, 210, 270 and 330 min. At t=90, 210 and 330 min micturition takes place and a portion of the urine is stored. Note the exact times of taking blood, times of urine discharges and urine volumes. During the entire investigation, the

patient should avoid standing as much as possible.

c. After centrifuging, two samples of plasma and two samples of urine (each 1,00 ml) are counted using a scintillation counter. A diluted standard (1:50 and 1:100) of the infused solution and a standard of ^{131}I are also counted in order to measure the amount of cross-talk from the ^{131}I to the ^{125}I channel.

d. After correction for background (plasma t=0) and the aforementioned cross talk, the ERPF is calculated from the measured samples:

* Constant infusion method (IFM):

ERPF = (I x F)/P (ml/min)

in which:

I = counts in 1,00 ml standard infusion (corrected for dilution)

F = infusion rate in ml/min

P = counts in 1,00 ml plasma

* Urine Collection Method (UCM):

ERPF = (U x V)/P (ml/min)

in which:

U = counts in 1,00 ml urine

V = urine production in ml/min

P = counts in 1,00 ml plasma

e. Only the last 2 collection periods are used for the UCM. For the IFM, only those plasma values are taken that remain constant over the course of time.

f. The ERPF value calculated by the UCM is only used to correct the GFR for inaccurate urine collection (see below). When the ERPF drops below 100 ml/min then the IFM ceases to be reliable even for hippuran (Iodohippurate ^{131}I solution) and only the UCM may be used.

g. The GFR may only be calculated using the UCM because iothalamate is also excreted extrarenally. When the ERPF calculated from the UCM differs from the ERPF calculated from the IFM, this indicates an error in urine collection which has a similar effect on the GFR calculated from the UCM. The GFR calculated from the UCM can be corrected for this by multiplying by the factor: ERPF calculated from IFM divided by ERPF calculated from UCM.

h. The FF is calculated from the ratio of the GFR to the ERPF.

Measuring conditions

Energy:	^{131}I-setting, 360 keV
	^{125}I-setting, 30 keV
Window:	20% for ^{131}I
	30% for ^{125}I
Counts:	Normally 5 min per sample is sufficient

10. Interpretation

a. The GFR and ERPF values are dependent on age. In childhood, correction for body surface area must be considered. The normal GFR is 120 ml/min, the ERPF 600 ml/min and the FF 0,20.
b. If repetition of the investigation is desired, it should take place with the patient in the same position as on the first occasion.
c. Important in carrying out the investigation are a high labelling percentage of the radiopharmaceutical (^{131}I and ^{125}I > 99,5%) and a constant level of the tracers during the investigation. If labelling is poor, the GFR and/or ERPF are undervalued: free iodine is cleared more slowly than the iothalamate or the hippuran.
d. If plasma concentrations are variable, the constant infusion method is unreliable.

11. Report

The absolute values of the GFR, ERPF and FF are recorded. Indicate whether or not these are corrected for body surface.

12. Literature

- Donker AJM, Van der Hem GK, Sluiter WJ, Beekhuis H. A radioisotope method for simultaneous determination of the glomerular filtration rate and the effective renal plasma flow. Neth J Med 1977;20:97-103.
- Dubovsky EV, Gates GF, Russell CD. Three approaches to computer-assisted function studies of the kidney and evaluation of scintigraphic method. In: Tauxe WN, Dubovsky EV, eds. Nuclear Medicine in Clinical Urology and Nephrology. Norwalk, Connecticut: Appleton-Century-Crofts;1985:157-89.
- Peters AM. Quantification of renal haemodynamics with radionuclides. Eur J Nucl Med 1991;18:274-86.
- Russell CD. Radiopharmaceuticals used to assess kidney function and structure. In: Tauxe WN, Dubovsky EV, eds. Nuclear Medicine in Clinical Urology and Nephrology. Norwalk, Connecticut: Appleton-Century-Crofts;1985:7-29.
- NKF KDOQI Guidelines: Clinical practice Guidelines for Chronic Kidney Disease: Evaluation, Classification and Stratification. American Journal of Kidney Diseases, 2002 feb; 39 (2, Sup).