Introduction to the Consensus Reports

The Radionuclides in Nephrourology Group consists of approximately 200 physicians and scientists from countries throughout the world who have been meeting on a regular basis approximately every three years since 1968. In 1992, the scientific committee of this Group, which is not affiliated with the Society of Nuclear Medicine, decided to establish three committees to develop consensus reports on the use of radionuclides to measure renal clearances, to detect renovascular hypertension and to detect obstructive uropathy. There were several factors that led to the decision to prepare these consensus reports. Widely varying technical procedures were being followed in all of these areas; different data were being collected, and it was often difficult to compare and interpret results from different centers. The scientific committee believed that some minimal standardization of procedures and protcols would enhance the utility of these tests, facilitate meta-analyses of the results and better identify problem areas. Second, the committee sought to raise the level of practice of renal nuclear medicine by clearly identifying specific procedures and interpretative criteria that are important in the performance of these tests. Third, a review of these areas by an international panel of experts should serve as a timely contribution to the field. The three consensus reports were formally presented at the Ninth International Symposium of Radionuclides in Nephrourology held in Santa Fe in May 1995. Attendees at the Symposium were invited to submit comments to the respective chairs. The reports were subsequently completed in the Fall of 1995 and submitted for review to *The Journal of Nuclear Medicine*. Although there will undoubtedly be overlap between these consensus reports which represent an international viewpoint and the practice guidelines currently under development by the Society of Nuclear Medicine, the consensus reports and the practice guidelines are entirely different documents with complementary but different objectives, different sponsoring organizations and different organizing panels.

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Consensus on Diuresis Renography for Investigating the Dilated Upper Urinary Tract

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There is great variation in technique and interpretation of diuresis renography between different establishments. **Methods:** To address this problem, an International Consensus Committee was appointed by the Ninth International Symposium on Radionuclides in Nephrourology in 1994. **Results:** The final document was produced and addressed: objectives, equipment, data acquisition, choice of radiopharmaceutical, patient preparation, position, dosage of furosemide, timing of furosemide, role of bladder catheter, duration of study, pediatric considerations, evaluation of the furosemide response, interpretation, and conclusion. **Conclusion:** The report presents a standardized approach to diuresis renography that, if adopted, will improve reproducibility between centers, discourage unacceptable practice and stimulate further discussion between nuclear medicine and urology health care professionals who treat patients with dilated and obstructed upper urinary tracts.

Key Words: diuresis renography; technetium-99m-MAG3; furosemide

J Nucl Med 1996; 37:1872–1876

Received Jan. 25, 1996; revision accepted July 22, 1996.
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Diuresis renography is widely accepted as a useful test for investigating the dilated urinary tract and discriminating between obstructed and nonobstructed systems (*1–5*). Unfortunately, there is still a great deal of variation in the performance and interpretation of the test between different centers (*6*). To address this problem, the Scientific Committee of the Ninth International Symposium on Radionuclides in Nephrourology established a Consensus Committee on Diuresis Renography in 1994. Members were nominated by the Scientific Committee or appointed by the chairperson. Several drafts were considered by the committee before the final document was considered at a meeting in Santa Fe, NM. This article incorporates the changes, suggestions and amendments that resulted from that discussion and subsequent correspondence.

BACKGROUND

There are many causes of dilatation of the upper urinary tract. It has become clear in recent years that not all of these are genuinely obstructive and a threat to renal function and health. Thus, the adage that "dilatation does not equal obstruction" has become an oft-repeated message. Static imaging methods tell

the clinician little about renal function and urodynamics. Only diuresis renography can provide information on both these parameters in one test (perfusion studies give no information on function and are not widely used in current clinical practice). Thus, it is imperative that techniques for the performance of diuresis renography are standardized, reliable and repeatable to give accurate results and allow comparison of reports from different centers. In this report, dilatation refers to any increase in dimension of the upper outflow tract (calices, pelvis, ureter) detected by intravenous urography or ultrasound. Obstructive uropathy refers to the effect of obstruction on the outflow tract, and obstructive nephropathy refers to the effect of obstruction on nephron function. Furosemide is the only diuretic considered.

OBJECTIVES

The objectives of this report are to standardize the technical aspects, performance and interpretation of diuresis renography in an effort to:

1. Ensure standardized protocols and improve reproducibility between different centers.
2. Highlight and examine variations from such protocol in the interests of discouraging unacceptable practice.
3. Stimulate further discussion within and between the nuclear medicine and urological communities.

COMMITTEE RECOMMENDATIONS

Choosing Hardware and Software

The choices of hardware and software can be left to individual centers but should include:

1. A large field-of-view gamma camera.
2. A low-energy, general-purpose collimator with a peak for ^{99m}Tc and a 20% window.
3. A special 160-keV collimator when ^{123}I-hippuran is used, although a general-purpose collimator will suffice.
4. A smaller detector for children and a smaller field-of-view camera for portable studies.

Data Acquisition

A 128 × 128 matrix size is recommended, although a 64 × 64 matrix is acceptable. For standard renography, a pixel depth of 8 bits is sufficient. The frame time should be in the range of 10–20 sec. Hard copy should include a number of high-quality morphological images and the renogram curve. A useful presentation is six serial 5-min images spanning the duration of the study along with the curves on an 8 × 10-in transparent film. Many centers have converted to digital archiving and display systems or print near-photographic quality studies on paper.

While the subject of background region of interest (ROI) often provokes lively debate, the committee agreed to recommend a C-shaped, elliptical perirenal ROI. Relative function is also a controversial area. The Well Tempered Diuretic Renogram (WTDR) group recommended the background subtracted integral of activity from between 60 sec after injection to the initial appearance of calyceal activity. Others suggest consideration of the ratio left/left+right during the first 3 min, or time to peak in the first kidney, or 1–3 min if neither kidney shows a peak.

This committee, in agreement with the Captopril Renography Consensus Committee, recommends integration of the background-subtracted renograms over 1–2 min or 1–2.5 min for OIH and MAG3. While it is recognized that the rapidly varying background may result in some inaccuracies in a small number of patients, this recommendation covers most clinical situations, reduces equivocal limits of integration and is the best consensus available. If DTPA is used, 2–3 min will be more appropriate.

Depth differences of >1 cm will lead to significant errors in the estimation of split renal function. In clinical practice, such differences are unusual, and there is no justification for routine measurement of kidney depth. Where ectopic or mobile kidneys are demonstrated, anterior and posterior views are required for accurate determinations.

Deconvolution analysis is not the brief of this consensus document; it is a useful technique for the measurement of parenchymal transit times for the assessment of obstructive *nephropathy*, rather than urodynamics, in cases referred for diuresis renography (*7–9*). Any department considering using deconvolution analysis where diuresis renography is equivocal must appreciate the considerable expertise required, and would be advised to visit an established center for advice.

Choosing the Radiopharmaceutical

Technetium-99m-mercaptoacetyltriglycine (MAG3) is the current agent of choice. It is predominantly secreted due to a high degree of protein binding with only a small amount being filtered (*10*). It has about 60% of the clearance of hippuran. It gives excellent images, including ureteric visualization in many cases, and produces crisp responses. The dosage is 70–120 MBq (~2–3 mCi).

Iodine-123-hippuran has been the gold standard renal radiopharmaceutical for the past twenty years. It is almost entirely secreted, so renal handling is fast and curve shapes and responses are crisp. The need for cyclotron production, and its short half-life and expense make distribution difficult and have restricted its widespread introduction. Where it is easily available, it can be recommended for use. The dosage is 20 MBq (~0.5 mCi).

Technetium-99m-diethylenetriaminepenta-acetic acid (DTPA) has been the most widely used renal radiopharmaceutical in the past. The advantages are cheapness, ease of production and intrinsic GFR measurement capability, but it is a slow, filtered agent with an increasingly poor target-to-background ratio in decreasing renal function that can make ROI mapping difficult. Its curve forms and diuretic responses are less immediate and more difficult to interpret than MAG3 and ^{123}I. It is not recommended for diuresis renography. The dosage is 70–120 MBq (app 2–3 mCi).

Patient Preparation

Send preattendance instructions to ensure that the patient is adequately hydrated. To avoid dehydration, the patient needs to maintain a 1–3 ml/min urine flow rate during the test. When the patient arrives, give the patient a 500-ml drink, such as water or orange juice, 15–30 min before examination. Some health care professionals recommend that the specific gravity of the urine voided pre-examination should be tested with results of less than 1.015 to ensure reliability.

Explain the renography procedure. If catheterization is not required, ensure that the patient voids before study. Urine output and the test duration should be measured at the conclusion of the study to determine urine production rates.

Patient Position

Supine. The patient is less likely to move or faint and kidney depth variation is minimized in this position.

Sitting Erect. The patient should preferably recline against the camera. There are normal hydrostatic effects on urine flow in this position.

Either position may be used and each has advantages, but the effect of posture on the dilated upper tract must be considered.

Moving the supine patient to the erect position during the examination, or repeating the examination erect after an initially supine study, may be necessary in some cases to clarify postural effects.

If a catheter was not used, postvoid images should be erect if possible and should always be obtained at the conclusion of the study to reduce equivocal results.

Furosemide Dosage and Timing

The dosage of furosemide is 1 mg/kg in infants, 0.5 mg/kg intravenously in children aged 1–16 yr and 40 mg intravenously in adults.

In standard diuresis renography, data are collected for 20 min before furosemide injection (F+20) to obtain unmodified data on uptake and elimination, and allow for slow elimination determined by the volume of high capacity, but nonobstructive, systems before the diuretic stimulus.

The maximal effect of furosemide is 15–18 min after intravenous injection, justifying the alternative method of giving the diuretic 15 min before the radiopharmaceutical (F-15). The F-15 timing is recommended where F+20 results are equivocal and/or renography under a state of maximal diuresis is required.

Some health care professionals administer the radiopharmaceutical and furosemide together (F+O), while others like to wait for high-capacity systems to fill completely before giving the diuretic, waiting for 20, 30 or even 60 min. If such individual variations are used, it is important to employ the F+ or F- system of documentation to inform other practitioners of the timing used, to standardize interpretation and to avoid confusion.

There are no data to support increasing the dose of furosemide in azotemic patients. Damaged tubules respond slowly and poorly to any dose; the diuresis renogram depends on a sudden, rapid diuretic response to produce an immediate, brisk stimulus to the outflow tract. Any increase in urine production by damaged tubules from large doses of furosemide tends to be a slow and more prolonged effect, and not one that produces the required acute stress to the obstructed segment.

Role of Bladder Catheter

A full or rapidly filling bladder, or a bladder with poor compliance, may affect upper tract emptying, giving false positive results for upper tract obstruction. Such results may be avoided by an indwelling open catheter, although this may not always be necessary. Suspected interactive effects of the bladder on renal emptying can be investigated by asking the patient to urinate 20 min into the test. Assuming no voiding dysfunction, the upper tracts' effects on bladder emptying will be reflected in the curves. Certain groups of patients, however, are unable to respond to this request and require an open indwelling catheter. These patients include those with lower tract obstruction, demonstrable postvoid residual urine, known voiding dysfunction, neuropathic bladders, vesicoureteric reflux and cases in which an unexpected obstructed curve is obtained.

Duration of Study

The recommended procedure is the traditional F+20 diuresis renogram, in which data are collected for 20 min followed by 15 min of further data acquisition after diuretic administration.

To avoid the need for the diuretic, some centers perform a 20-min unmodified study with postvoid images, preferably erect, especially if the original test was supine. If obstruction is excluded at this point, the test is terminated without proceeding to a diuretic phase. This may be acceptable in experienced hands but, if doubt exists, furosemide must be given and data collected for a further 15 min.

In some patients, initially rapid elimination in response to furosemide gives way after a short time to a sudden cessation of elimination or reversion to a rising curve, a response known as Homsy's, or delayed double-peak, sign (*11*), which is an indicator of intermittent hydronephrosis. Such a response always occurs 10–15 min after furosemide administration, which is why data collection should continue for 15 min after the diuretic is administered. If doubt regarding its interpretation exists, it should be clarified by a F-15 study, as described below.

Maximal diuretic effect occurs 15 min after furosemide, so a single-step, maximal diuresis renogram test can be performed administering the diuretic 15 min before the radiopharmaceutical (F-15) and continuing data collection for another 20 min. This variation results in identical split-function results as the F+20 technique. This method is recommended when the F+20 study is equivocal, or as a one-stop maximal-diuresis renogram instead of the traditional F+20 technique.

Pediatric Considerations

Dosage reductions for children should be based on surface area criteria, but with administered activity not less than 10% of the adult dose. There are few problems with pediatric diuresis renography, except for at the neonatal level, where some difficulties emerge. While split renal function determinations are reliable, washout interpretation is controversial. Renal physiology in the neonate is far removed from the adult, with glomerular filtration rate (GFR) rising only slowly from 40 ml/min/1.73 m^2 at 1 wk to 120 ml/min/1.73 m^2 at 2 yr. In addition, there are differences in renal blood flow, urinary concentrating ability and sodium reabsorption, all of which can affect diuretic handling and response. It has been suggested that in neonates and infants, renogram normalization between right and left, and conversion of transiently hydronephrotic curves to spontaneous normality, not occur before 4 mo, which makes washout interpretation in infants difficult before this age. Conversely, many workers rightly use the technique in neonates and report useful results. In particular the introduction of MAG3 has resulted in excellent images and reliable data in neonates, and a negative test for obstruction in this age group can be vital in decision making.

The best guidelines for diuresis renography in neonates have been those published by the joint consensus report of the Society for Fetal Urology (SFU) and the Pediatric Nuclear Medicine Council (PNMC) of the Society of Nuclear Medicine, known as the Well Tempered Diuretic Renogram (WTDR) (*12*). The main points are described below.

WTDR Patient Preparation. The patient should be at least 1 mo old. Serum creatinine should be measured to exclude azotemia. Oral hydration should be given ad libitum, as formula or water, beginning 2 hr before the study. Intravenous fluid should be given as dilute saline solution at 15 mg/kg over a 30-min period beginning 15 min before radiopharmaceutical administration. The patient's bladder should be catheterized (8F) to ensure adequate drainage throughout and minimize micturition movement. Bladder urine drainage should be measured at 10-min intervals to determine the diuretic response.

WTDR Renogram Technique. Technetium-99m-MAG3 is recommended at a dose of 50 μCi/kg and a minimum of dosage of 1 mCi. The patient should be supine. Both digital data acquisition, at 20 sec/frame, and analog images should be collected. Digital data should be collected in a 128 × 128 matrix for ease of ROI placement. ROI for background subtraction should be 2 pixels wide around the outer perimeter of

the ROI of the kidney. The renogram should continue for a minimum of 30 min.

WTDR Diuretic. Furosemide (1 mg/kg at 20 min, or when the entire collecting system is judged to be full) should be used.

WTDR Data Analysis. Data analysis should include: percent differential function; percent differential cortical function; 20 min to peak ratios; renogram curve pattern categories of normal, immature, stasis, obstructive and poor function; and clearance half-times for diuretic response analysis.

Consensus Committee Comments

This neonatal protocol was designed to ensure uniformity of technique and to reduce variations in the management of the newborn with obstructive uropathy. As such, it is rigid and unequivocal, but adherence to it should allow the technique to address even the most difficult cases. However, some points in the protocol deserve comment, and have not been addressed or revisited by the WTDR group at this time.

Neonates are by definition less than 1 mo old, so the WTDR recommendations really refer to infants, i.e. children up to 1 yr of age. However, even in children aged 1 mo or less, the negative predictive value of a normal diuresis renogram is high and clinically useful. Equivocal or positive studies may be nondiagnostic but will identify the need for serial follow-up. The technique should be available for children less than 1 mo old.

The committee questions whether it is really necessary to give an intravenous infusion to all neonates and infants to hydrate them. At what age does this become unnecessary? The committee also questions whether the bladder must be catheterized in all children. It may be essential in a referral population with a high pretest probability of urethral, bladder or ureteric dysfunction (neonates), but not necessarily in older children.

The intent of the WTDR was to ensure that all variables were addressed in one test. This may result in overkill, but in some departments where physician attendance, technologist training and monitoring of patient preparation is suboptimal, adherence to its recommendations must be justified. It is hoped that the WTDR group will revisit and update their report to clarify the above points.

Evaluation of the Furosemide Response

The major determinants of furosemide response are the level of renal function and the volume of the collecting system. Poor function (<15 ml/min single kidney glomerular filtration rate {SKGFR}) and huge-capacity systems represent the major causes of false-positive (poor washout) results (*13,14*).

False-negative results are less common but can occur in highly compliant (small volume, tight) renal pelves, or when there is powerful high-pressure diuresis through partially obstructed systems.

Stepwise or irregular curves can occur from fluctuations in blood flow, vesico-ureteric or uretero-ureteric (duplex systems) reflux, or as a secondary rise (Homsy's sign) associated with intermittent hydronephrosis.

Visual interpretation of the curves is accurate in the overwhelming majority of cases.

The use of various reported half-times or diuresis excretion indices vary with radiopharmaceuticals, renogram technique and software; tend to be institution-specific; and are not easy to reproduce between departments. At least seven different methodologies have been reported to quantify half-time. In spite of these, 85% of patients of F+20 diuresis renography, and 93% of patients in whom F-15 diuresis renography is performed in equivocal cases, are resolved without such assistance.

Interpretation

In general, the following advice can be given. A normal response should be interpreted as normal.

An obstructed response with a SKGFR >15 ml/min should be considered obstructed.

A response of SKGFR <15 ml/min requires caution. Poor diuretic response is likely. F-15 is unlikely to be helpful. Consider parenchymal transit time or perfusion pressure flow studies. Check symptoms and split renal function. Examine clinical status and indications for intervention.

A nonobstructive response is almost certainly not obstructed at that flow rate. Rarely, there may be some degree of obstruction that might be overcome by high-pressure diuresis within a noncompliant renal pelvis to produce good washout. Examine the curves. Investigate further if the result is inconsistent with clinical impressions and an F-15 study is recommended.

An equivocal response of SKGFR >15 ml/min indicates diuresis is probably good. Some degree of obstruction is likely but not necessarily worthy of intervention. Examine split function and clinical status.

A true equivocal result of SKGFR <15 ml/min should be described as such, and not as partial obstruction. In such cases the questions to be asked are:

1. What was the renal function?
2. What was the system volume?
3. What position was used?
4. What was the state of hydration?
5. Was there any bladder abnormality?
6. Were the consensus guidelines observed?

When all these conditions have been satisfied, further investigation is required. F-15 diuresis renography is unlikely to help. Consider all available features: clinical, bacteriological, value of perfusion pressure flow studies and best interest of the patient. Other methods of clarification might then include: measurement of outflow efficiency (15); measurement of the parenchymal transit time index (*16*); and perfusion pressure flow studies in some selected cases (*17*).

CONCLUSION

Standardization of diuresis renography is long overdue. In conjunction with the recommendations for neonates in the Well Tempered Diuretic Renogram, we hope that these guidelines on diuresis renography from the Consensus Committee of the Society for Radionuclides in Nephrourology will be useful to nuclear medicine practitioners, urologists and radiologists interested in pursuing accuracy and reproducibility in their investigations of obstructive uropathy.

ACKNOWLEDGMENTS

We thank Dr. Andrew Hilson of London, England, Lieutenant Colonel Mike McBiles, US Army, Colorado and Dr. George Sfakianakis of Miami, Florida for their valued input.

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Consensus Report on ACE Inhibitor Renography for Detecting Renovascular Hypertension

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Key Words: ACE inhibitor; renography; renovascular hypertension

J Nucl Med 1996; 37:1876–1882

The primary purpose of this consensus report is to assist nuclear medicine physicians in performing and interpreting angiotensin converting enzyme inhibitor (ACEI) renography for the evaluation of patients with suspected renovascular hypertension. The secondary purpose is to provide guidelines for future publications and to suggest directions for future research.

CONSENSUS PROCESS

There is considerable variation in the performance and interpretation of ACEI renography between different centers. This variation often makes it difficult to compare results and can lead to confusion regarding what procedures should be followed and what interpretative criteria should be applied. To address these problems, the Scientific Committee of the Ninth International Symposium on Radionuclides in Nephrourology established a Consensus Group on ACEI renography. Members of the Consensus Group consisted of those nominated by the Scientific Committee or selected by the chair.

The Delphi process was used as a guide to developing consensus (*1*). A preliminary list of statements regarding ACEI renography was submitted to the panel members, of whom each was asked to rate each statement from 1 to 10 on the basis of importance. Panel members were also invited to comment on the adequacy of the statements. A number of specific questions were raised as well as the methodological question of evaluating statements based on importance compared with agreement. In response to these questions, two detailed lists were prepared each containing approximately 150 statements. These lists were sent to the panelists and each panelist was asked to score the statements on one list on the basis of importance and score the second list on the basis of agreement. The scores were tabulated and a mean and s.d. were calculated for each statement. The anonymous individual scores, means and s.d.s of all the previous statements as well as a draft document based on the first round of scoring were sent to all panelists. The panelists were then asked to score the original statements again as well as to score a set of additional statements added to clarify ambiguities; panelists were also asked to comment on the draft. Based on the second round of scores and comments on the initial draft, the consensus report was redrafted and submitted to all the panelists as well as to all attendees at the Ninth International Symposium on Radionuclides in Nephrourology, which was held in Santa Fe, New Mexico, May 1–3, 1995. There was a 30-min presentation of the consensus report at the Symposium followed by one hour of open discussion. Subsequently, several

Received Feb. 2, 1996; revision accepted Feb. 28, 1996.
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