Normalized Residual Activity: Usual Values and Robustness of the Method

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The objectives of this study were 2-fold: first, to investigate the robustness of the normalized residual activity (NORA), a parameter that has recently been proposed for the estimation of renal emptying during renography; and second, to define the usual values of NORA in 2 categories of kidneys—those with a normal renogram and those that are dilated but definitely unobstructed. **Methods:** NORA was defined as the renal activity at a given moment (end of renogram, end of furosemide acquisition, image after micturition) divided by the renal activity between 1 and 2 min. Two variables that might influence the results of NORA were evaluated: the choice of background correction, and an error in the estimation of the 1- to 2-min renal activity. To estimate the values of NORA in usual clinical conditions, 2 sets of data were analyzed: normal kidneys with a normal renogram pattern, and dilated but definitely unobstructed kidneys. **Results:** Using a perirenal or a subrenal background correction, NORA was, on average, 67% or 83%, respectively, of the value obtained without background correction. The use of a renal activity of 1 min 20 s to 2 min 20 s instead of a 1- to 2-min activity resulted in a systematic 10%–15% underestimation of NORA. The 90th percentile values of NORA were, in the normal group, 0.70 at 20 min, 0.23 at the end of the furosemide test, and 0.10 after micturition. In the kidneys that had undergone surgery, the 90th percentile values were 3.92 at 20 min, 2.91 at the end of the furosemide test, and 1.99 after micturition. A good correlation was observed between NORA and output efficiency. **Conclusion:** If adequately standardized, NORA is a robust and simple parameter that allows evaluation of renal emptying at any time of the acquisition. One should be aware of the fact that high NORA values, corresponding to poor renal emptying, may be observed in the operated unobstructed kidneys, even after micturition.

Key Words: renogram; normalized residual activity; renal drainage; renal output; hydronephrosis

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A new parameter, normalized residual activity (NORA), has recently been proposed, allowing the estimation of renal emptying during renography, with or without additional furosemide stimulation (*1*). This very simple parameter is, like output efficiency (OE), correlated with the true mean transit time (*1*). The aim of this paper was 2-fold: first, to investigate the robustness of NORA (i.e., the factors that may affect the value of this parameter); and second, to define the usual values of NORA in 2 categories of kidneys—those with a normal renogram and those that are dilated but definitely unobstructed.

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MATERIALS AND METHODS

Renographic Studies

Acquisition. The patient was in supine position and placed above the gamma camera. ^{99m}Tc-Mercaptoacetyltriglycine (MAG3) was administered intravenously at a maximal dose of 100 MBq, scaled on a body-surface basis (*2*). A 20-min renogram acquisition was obtained, using 20-s frames. The computer was started at the moment the activity entered the field of view of the gamma camera. At 20 min, a dose of furosemide was administered (1 mg/kg of body weight; maximum, 20 mg) and a new 15-min acquisition was started; no indwelling bladder catheter was used. In the case of incomplete renal emptying at the end of the acquisition, the patient was asked to empty his or her bladder (in small noncooperative children, spontaneous bladder emptying always occurred within 15 min after the end of the acquisition), and an image was obtained after micturition between 50 and 60 min after tracer injection. This late image included the effect of gravity because the patient was encouraged to walk after the end of the furosemide acquisition. Small children were held vertically in the arms of the parent.

Processing. Rectangular renal regions of interest (ROIs) were drawn. The renal curves were corrected for background using a perirenal area; the heart curve was obtained by drawing, on the early image, an ROI around the highest heart activity.

Split renal function was classically determined on the basis of the 1- to 2-min background-corrected renal activity (*3*).

T_{max} was the time to reach the maximal activity on the renogram.

NORA was defined as the ratio between a 1-min renal activity at a given moment and the renal activity between 1 and 2 min (R2). NORA was calculated at 3 moments of the acquisition: R (end of renogram)/R2, R (end of furosemide test)/R2, and R (after micturition)/R2.

OE was calculated according to previous publications (*4–7*). The integral of the heart curve was adjusted to the early part of the corrected renogram (between 1 and 2 min). The difference between the integral of the heart curve up to the end of the furosemide acquisition and the 1-min renal activity at the same time represents what has left the kidney. This difference was expressed in the percentage of the integral of heart activity.

TABLE 1
Effect of Renal Background Correction on NORA in 22 Patients

Background correction	NORA (mean ± SD)
None	100 ± 0
Perirenal	67 ± 9
Subrenal	83 ± 5

Robustness of NORA

To test the robustness of NORA, 2 factors that may influence the result of this parameter were evaluated.

Effect of Background Correction. Background correction modifies the net renal uptake at 2 min, whereas, because of the small distribution volume of MAG3, it only slightly affects the late renal counts.

To test the effect of background on the value of NORA, 2 background ROIs were selected for each kidney: a 1-pixel-wide perirenal background, drawn around the renal ROI; and a subrenal ROI. Each of these background areas was normalized to the size of the kidney ROI. NORA was calculated on 22 patients (7 adults and 15 children who were >2 y old). All patients had a normal or moderately impaired overall renal function (^{51}Cr-ethylenediaminetetraacetic acid [EDTA] clearance between 70 and 197 mL/min/1.73 m^2). NORA was calculated without any background correction and using either a perirenal or a subrenal area for background correction.

Effect of Error on Estimation of 2-min Renal Activity (R2). Ideally, the time zero of the renogram should be standardized and can, for instance, be defined as the moment at which the tracer reaches the heart. In clinical practice, however, the computer is started more or less at the time the tracer is injected. This may give rise to some uncertainty in the estimation of R2 because of the variable circulation time between the injection site and the heart and because of the variable delay in computer response. Therefore, NORA was also calculated using for R2 the renal activity between 1 min 20 s and 2 min 20 s, considering that the maximal potential error on the estimation of R2 was one 20-s frame. In 162 patients (84 children [age, 15 d to 15 y; median age, 3.3 y] and 78 adults [age, 19–83 y; median age, 53 y]), the results of NORA, using the renal activity at either 1–2 min or at 1 min 20 s to 2 min 20 s, were compared. In these patients, the glomerular filtration rate of the single kidney was estimated by combining the overall ^{51}Cr-EDTA clearance with the ^{99m}Tc-MAG3 split renal function. The range of values was between 5 and 97 mL/min/1.73 m^2.

Usual Values for NORA

Normal Kidneys. These kidneys were from 136 children (age, 15 d to 15 y; median age, 8.2 y) and 39 adults, in total 175 kidneys. They were selected on the basis of absence of underlying pathology and were on the contralateral side of an abnormal kidney. An additional inclusion criterion was a normal renogram, arbitrarily defined on the basis of a T_{max} of <7 min. Moreover, in 42 of these kidneys, the response to furosemide administration and micturition was available because of the pathology of the contralateral kidney.

Unobstructed Dilated Kidneys. These kidneys were from 74 children (age, 15 d to 15 y; median age, 5.1 y) and 8 adults, in total 82 kidneys. These patients underwent a MAG3 renogram at least 1 y after pyeloplasty was performed because of unilateral pelviureteric junction stenosis.

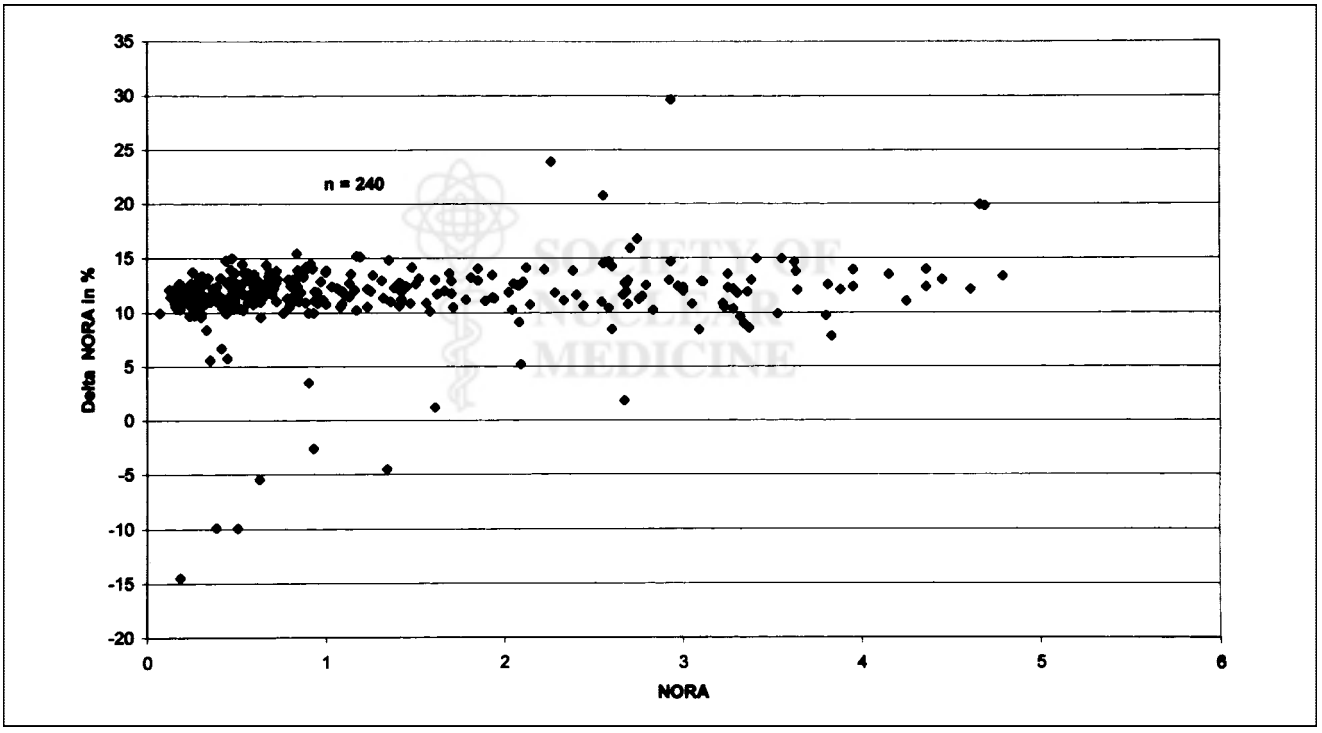

FIGURE 1. Bland–Altman plot shows effect of 20-s error on determination of NORA. Value of NORA is given on abscissa; difference (%) between NORA calculated using 1- to 2-min renal activity and using renal activity of 1 min 20 s to 2 min 20 s is shown on ordinate.

RESULTS

Robustness of NORA

The effect of renal background correction on NORA is shown in Table 1. Using a perirenal or a subrenal background correction, NORA was, on average, 67% or 83%, respectively, of the value obtained without background correction. Individual values fluctuated between 40% and 90%.

A Bland–Altman plot (Fig. 1) shows the effect of a 20-s error on the determination of NORA. The use of a renal activity of 1 min 20 s to 2 min 20 s instead of a 1- to 2-min activity resulted in a systematic 10%–15% underestimation of NORA. All differences of >15% were related to low single-kidney glomerular filtration rates (<20 mL/min/1.73 m^2) and a poor signal-to-noise ratio.

Usual Values for NORA

Figure 2 shows the distribution of NORA values. In the normal kidneys, NORA at 20 min was almost always <1.0. No clear differences related to age were observed. In the kidneys that had undergone surgery, NORA at 20 min was only rarely in the normal range and was primarily >2.

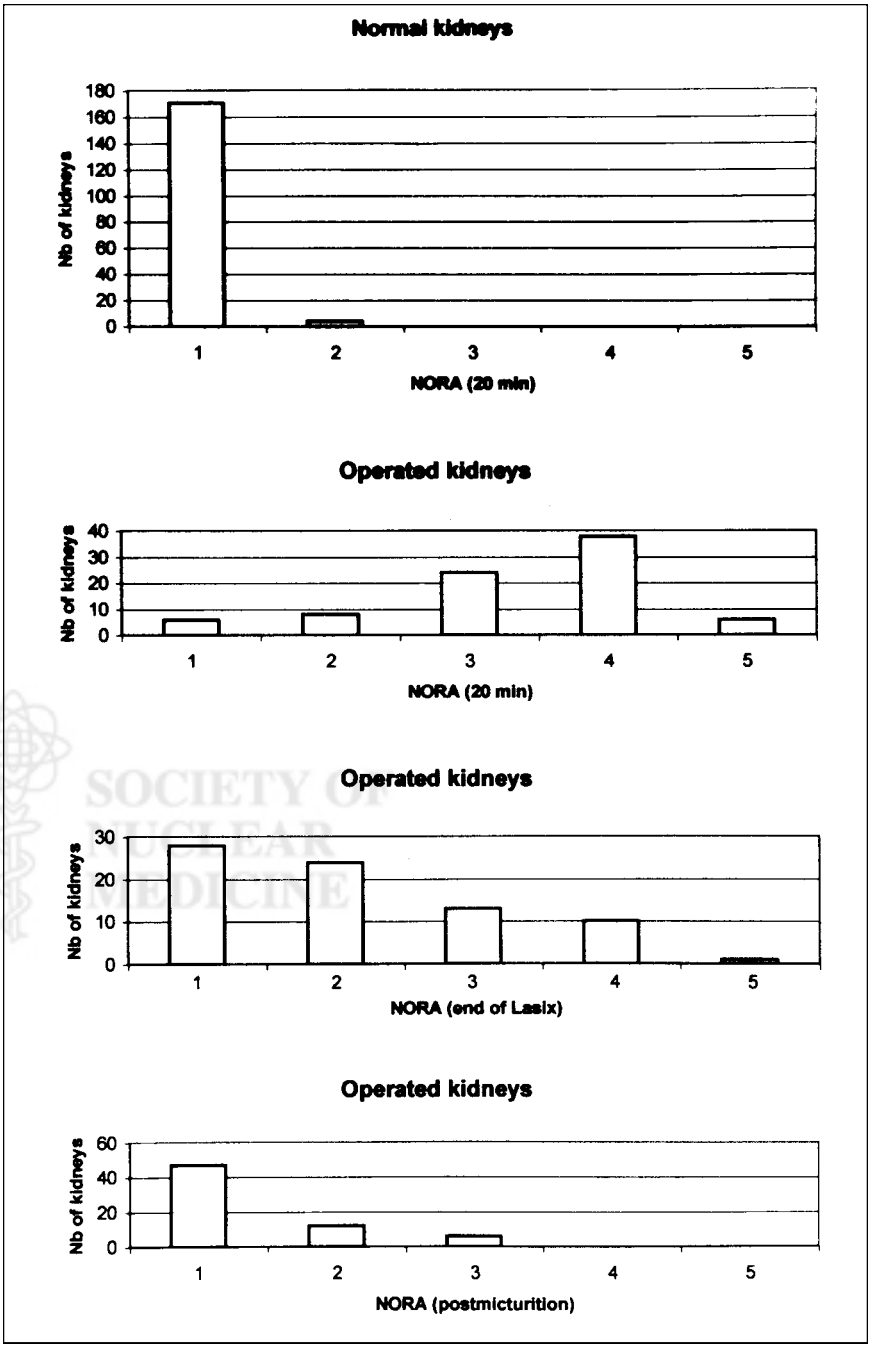

FIGURE 2. Histograms of NORA values for normal kidneys (at 20 min) and for kidneys with pelviureteric junction stenosis that had undergone surgery (at 20 min, at end of furosemide [Lasix; Hoechst Marion Roussel SA, Brussels, Belgium] acquisition, and after micturition). Five categories of NORA values (0–1, 1–2, 2–3, 3–4, and 4–5) are given on abscissa; number (Nb) of kidneys for each category is given on ordinate.

TABLE 2
NORA: 90th Percentile Values

Kidneys	*n*	Timing for NORA	P90
Normal	175	20 min	0.70
	42	End of furosemide	0.23
	42	After micturition	0.10
Previous surgery	82	20 min	3.92
	75	End of furosemide	2.91
	65	After micturition	1.99

P90 = 90th percentile.

NORA at the end of the furosemide acquisition, and even after micturition, was still out of the normal range in most kidneys. Table 2 shows the 90th percentile values of NORA. In the normal group, it was 0.70 at 20 min, 0.23 at the end of the furosemide test, and 0.10 after micturition. In the kidneys that had undergone surgery, it was 3.92 at 20 min, 2.91 at the end of the furosemide test, and 1.99 after micturition.

Figure 3 shows the comparison between NORA values at the end of the furosemide acquisition and on late images obtained after attaining an erect position and micturition. A striking decrease of NORA was often observed after micturition, but incomplete renal emptying was still found in a large number of patients.

Figure 4 shows the correlation between NORA calculated at the end of the furosemide acquisition and OE. A good correlation was observed between both parameters (R^2 = 0.917).

DISCUSSION

Several methods allow the evaluation of renal drainage, the most widely used being the stimulation by means of furosemide. It is now well understood that evaluation of the response to furosemide in a child should include images after micturition, after change in the child's position (erect position), thus avoiding the effect of a full bladder when no bladder catheter is used and the residual renal stasis related to the supine position. Quantitative parameters based on this late image might reveal a much better drainage than any parameter derived from the furosemide acquisition.

OE (*4*–*7*) and NORA (*1*,*8*) have been proposed for quantification of the renal emptying. These 2 parameters can be determined at any moment of the acquisition, in particular at the end of the renogram, at the end of the furosemide acquisition, or on the image after micturition. They are a pure expression of what has left the kidney during the whole acquisition (*1*).

NORA has the advantage of being an extremely simple parameter that does not necessitate any particular processing. It is a better parameter than T_{max} and residual activity expressed as a percentage of the maximal activity because it

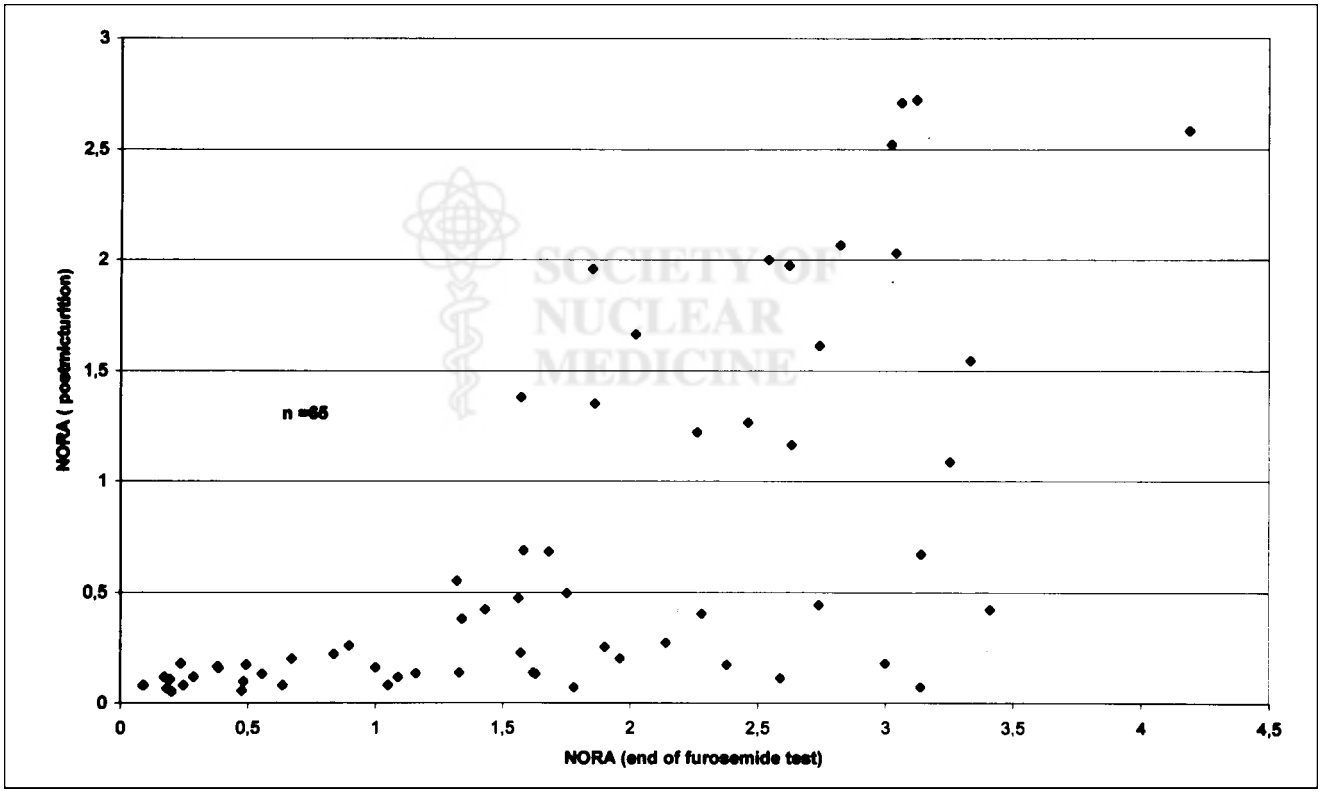

FIGURE 3. Comparison of NORA values obtained at end of furosemide acquisition and after micturition.

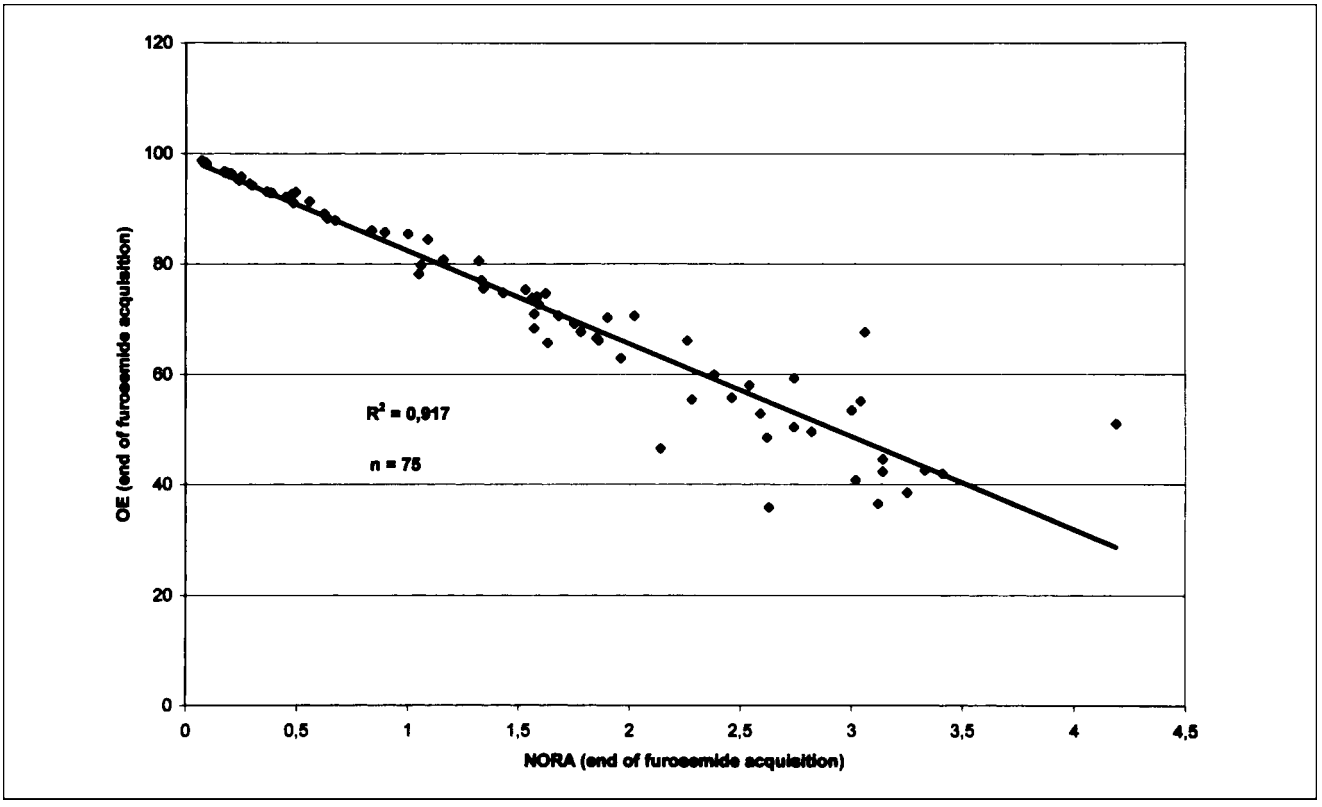

FIGURE 4. Correlation between NORA and OE calculated at end of furosemide acquisition.

takes into account the value of renal clearance (*1*). As shown in this study, it can be affected by 2 variables. The choice of background clearly influences the results of NORA and should therefore be standardized. The 10%–15% systematic bias introduced by an error in the appreciation of the timing of the beginning of the renographic acquisition (and therefore on R2) is clearly exaggerated because the error on timing is unlikely to reach 20 s. If the computer is started systematically at the moment the tracer reaches the field of view of the gamma camera, this error is reduced to only a few seconds. OE can also be affected by factors such as the choice of background or the choice of a heart curve instead of a true plasma curve (*7*). Therefore, standardization of both parameters is mandatory to be able to compare the results obtained at different centers.

When defining a new parameter, determination of the normal values is mandatory. However, in kidneys for which there is a high suspicion of obstruction, the renal outflow parameters should be compared with those of dilated but definitely unobstructed kidneys rather than with those of obviously normal kidneys. This comparison explains the selection of patients in our study. Under the conditions of this study, a value of <1.0 at the end of the 20-min renogram can now be considered as corresponding to a good renal drainage. The normal upper limit reaches 0.23 at the end of a furosemide acquisition and reaches 0.10 after micturition. It is not surprising that high NORA values were observed in the group of kidneys that had successfully undergone surgery, at the end of the renogram, at the end of the furosemide acquisition, and even after micturition and the effect of gravity. Indeed, most of these kidneys remain dilated despite successful surgery, and the poor renal emptying reflects only the stasis in these dilated cavities. This wide range of values is not specific for NORA. As shown in Figure 4, NORA and OE at the end of the furosemide acquisition were closely correlated, and OE values of <60 were found in a significant number of kidneys that had successfully undergone surgery.

CONCLUSION

If adequately standardized, NORA is a robust and simple parameter, allowing the evaluation of renal emptying at any time of the acquisition. Additional work is needed to compare the values found in well-defined unobstructed groups with the values found in selected populations that are highly suspected of having obstruction.

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