Influence of Renal Function on Renal Output Efficiency

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The purpose of this study was to quantify the influence of renal function on output efficiency (OE) and to evaluate factors that may modify this effect. **Methods:** Renograms were generated in a computer simulation model by convolution of plasma disappearance curves with artificially created retention functions. Ten plasma curves were derived from a database corresponding to renal clearances ranging from 33 to 405 mL/min. The created retention functions had 3 characteristics: (*a*) no output until the minimal transit time (MinTT) followed by a linear increase in transit time; (*b*) ratio of MinTT to mean transit time (MTT) equal to 0.3 or 0.8; and (c) MTT between 3 and 60 min, increasing with 1-min steps. For each of the 1,160 renograms generated, output efficiency at time (*t*), OE_t, was calculated at 20, 40, and 60 min. Mean and SD of OE_t for all clearances were calculated for MTT values between 5 and 60 min, increasing with 5-min steps. **Results:** For the same retention function, different clearances resulted in different values of OE_t. The degree of variability of OE_t depended on several factors, including the value of *t*, the value of MTT, and the shape of the retention function, expressed as the MinTT-to-MTT ratio. For OE_{20}, OE_{40}, and OE_{60}, the respective maximum SDs were 5.4%, 6.6%, and 7.1% for retention functions with a MinTT-to-MTT ratio equal to 0.3, and 6.2%, 8.4%, and 9.4% for retention functions with a MinTT-to-MTT ratio equal to 0.8. **Conclusion:** OE is influenced by renal function. Care should be taken in establishing the cutoff values for obstruction, nonobstruction, and the nondiagnostic zone, since a change in overall clearance can cause as much as a 20% variation in OE.

Key Words: renography; output efficiency; renal function; simulation study

J Nucl Med 2002; 43:851–855

Transit evaluation is one of the main applications of radionuclide tests in nephro-urology, and the calculation of output efficiency (OE) may be the method of choice for this purpose (*1–4*). Unlike the deconvolution technique, OE may be applied to a nonstationary system, hence it can be calculated at any time during the renogram, after the furosemide test, or after the postmicturition image (*5*,*6*). Compared with the classical furosemide curve analysis, OE has the advantage of being independent of renal clearance, at least according to some researchers (*6*). However, Fleming et al. (*7*) showed that renal clearance did influence the value of OE. The aim of this study was to quantify the influence of renal function on OE and to analyze the factors that may modulate this effect.

MATERIALS AND METHODS

A series of renograms, $R(i)_{n,m}$, were generated in a computer simulation model by convoluting real input functions, $P(i)_n$, with artificial retention functions, $H(i)_m$, in accordance with the equation:

$$R(i)_{n,m} = P(i)_n * H(i)_m, \qquad \text{Eq. 1}$$

which, for discontinuous sampling methods can be written as:

$$R(i)_{n,m} = \sum_{j=0}^{j=i} P(i)_n.H(i-j)_m, \qquad \text{Eq. 2}$$

with *i*, the frame number, running from 1 to *N*, the total number of frames.

Time per frame and *N* were respectively set at 10 s and 720, resulting in a simulated acquisition of 120 min.

Plasma disappearance curves, $P(i)_n$, of the renal tracer served as input function, which for discontinuous sampling methods can be expressed as (*8*):

$$P(i)_n = \alpha_{1,n}.e^{-i.\lambda_{1,n}} + \alpha_{2,n}.e^{-i.\lambda_{2,n}}. \qquad \text{Eq. 3}$$

The values for percentage of injected dose, $\alpha_{1,n}$ and $\alpha_{2,n}$, and the rate constants $\lambda_{1,n}$ and $\lambda_{2,n}$ were derived from plasma disappearance curves of ^{99m}Tc-MAG_3 obtained in 10 patients chosen from our database. These plasma curves corresponded to renal clearances ranging from 33 to 405 mL/min, and increasing with approximately 40 mL/min intervals.

Two sets of retention functions were created. For the first set, the ratio of minimal transit time (MinTT) to mean transit time (MTT) was arbitrarily set at 0.3; for the second set, this ratio was arbitrarily set at 0.8. For each set, the MTT of the retention functions was set between 3 and 60 min, increasing with 1-min steps and resulting in 58 values for MTT. In this model we have disregarded the vascular phase; $H(0)$ (the retention at $i = 0$) is

Received Oct. 9, 2001; revision accepted Feb. 19, 2002.

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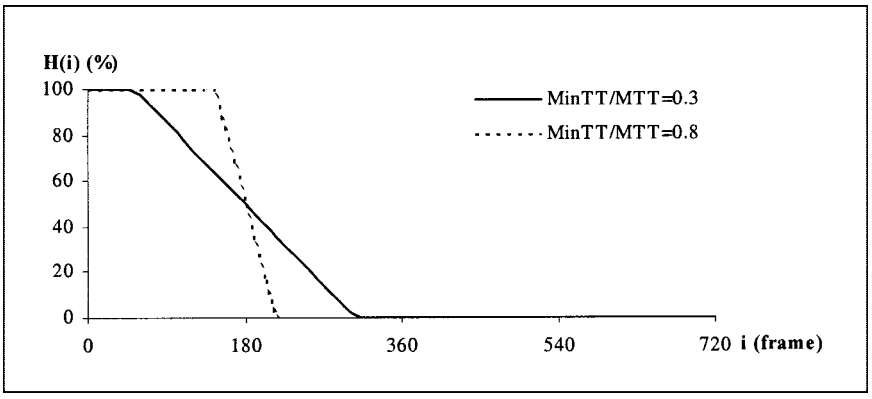

FIGURE 1. Two retention functions at MTT = 30 min. Solid line represents MinTT = 9 min, MaxTT = 51 min; dotted line represents MinTT = 24 min, MaxTT = 36 min.

therefore equal to 1. Subsequently, for each set and for every value of MTT, a retention function was created in a spreadsheet program (Microsoft Excel) reflecting a multinephron model with no output until MinTT, followed by a linear increase in transit time (Fig. 1) to the maximal transit time (MaxTT). Finally, each of the 116 retention functions, *m*, was convolved with each of the 10 plasma disappearance curves, *n*, and 1,160 renograms, $R(i)_{n,m}$, were created.

For every $R(i)_{n,m}$, the $OE_{n,m,t}$ was calculated for *t* equals 20, 40, and 60 min according to the formula:

$$OE_{n,m,t} = \frac{\text{Total output for } R_{n,m} \text{ up to } t}{\text{Total input of } P_n \text{ up to } t}, \qquad \text{Eq. 4}$$

which, expressed as a percentage, equals:

$$OE_{n,m,t} = 100\% \cdot \left[\frac{\sum_{t=0}^{t} P(i_t)_n - R(i_t)_{n,m}}{\sum_{t=0}^{t} P(i_t)_n}\right] = 100\% \cdot \left[1 - \frac{R(i_t)_{n,m}}{\sum_{t=0}^{t} P(i_t)_n}\right]. \qquad \text{Eq. 5}$$

The nominator of Equation 5, at *t* equals 20, 40, and 60 min, was calculated as the sum of frames 115 to 120, 235 to 240, and 355 to 360, respectively, of $R(i_t)_{n,m}$, and the denominator was calculated as the sum of frames 1 to 120, 1 to 240, and 1 to 360, respectively, of $P(i_t)_n$.

For each retention function, *m*, 10 values of $OE_{n,m,t}$ were calculated at a single time, *t*. Mean and SD of each value of $OE_{n,m,t}$ were calculated.

The relationship between mean and SD of OE_t to MTT was expressed graphically; the former reflects the general tendency of OE_t to MTT, while the latter reflects the variability of OE_t induced by renal clearance.

RESULTS

As expected based on a previous study (*9*), the value of OE_t varied depending on the value of *t*, the time of measurement. A nonlinear relationship was observed between OE_t and MTT (Fig. 2).

For each retention function *m*, the 10 plasma disappearance curves with different clearances resulted in renograms with different values for OE_t, suggesting that renal function did influence OE. However, the degree of its effect was not constant. As shown in Figure 2, the SD of OE_t was dependent on the values of *t* and MTT and the ratio of MinTT to MTT. This variation is more clearly shown in Figure 3, where the SD is presented against MTT. Moreover, in this figure, the variability of OE_t when plotted against MTT follows the same shape whatever the value of *t*. It is low for very short MTT, increases with higher values of MTT until reaching a maximum, and decreases with increased values of MTT.

The location and degree of the maximum variability depend on the value of *t*. The maximum variability appeared at lower values of MTT for OE_{20} than for OE_{60}, and the maximum variability of OE_{20} was lower than that of OE_{60}.

At all values of *t*, the highest variability of OE_t occurred when changes of OE_t closely followed changes in MTT. This is seen by comparing Figure 2 and Figure 3. For example, Figure 3 shows that the highest variability for OE_{20} is observed at MTT = 10 min, whereas Figure 2 shows that a close relation between OE_{20} and MTT exists around the value of MTT = 10 min. The variability of OE_t was also modulated by the shape of the retention function (when Fig. 3A is compared with Fig. 3B). For each OE_t the shape of the SD curve follows the same general pattern, with an initial increase, a maximal value, and finally a decrease. However, the height and the spread of the SD curve varied as a function of OE_t. The maximal variability was systematically higher in retention functions with a higher MinTT-to-MTT ratio. When compared with retention functions with a low MinTT-to-MTT ratio, the maximal variability occurs systematically at a higher value of MTT.

Quantitatively, the influence of renal function on OE was significant (Fig. 3). For OE_{20}, OE_{40}, and OE_{60}, the maximum respective SDs observed were 5.4%, 6.6%, and 7.1% for a MinTT-to-MTT ratio equal to 0.3, and 6.2%, 8.4%, and 9.4% for a MinTT-to-MTT ratio equal to 0.8.

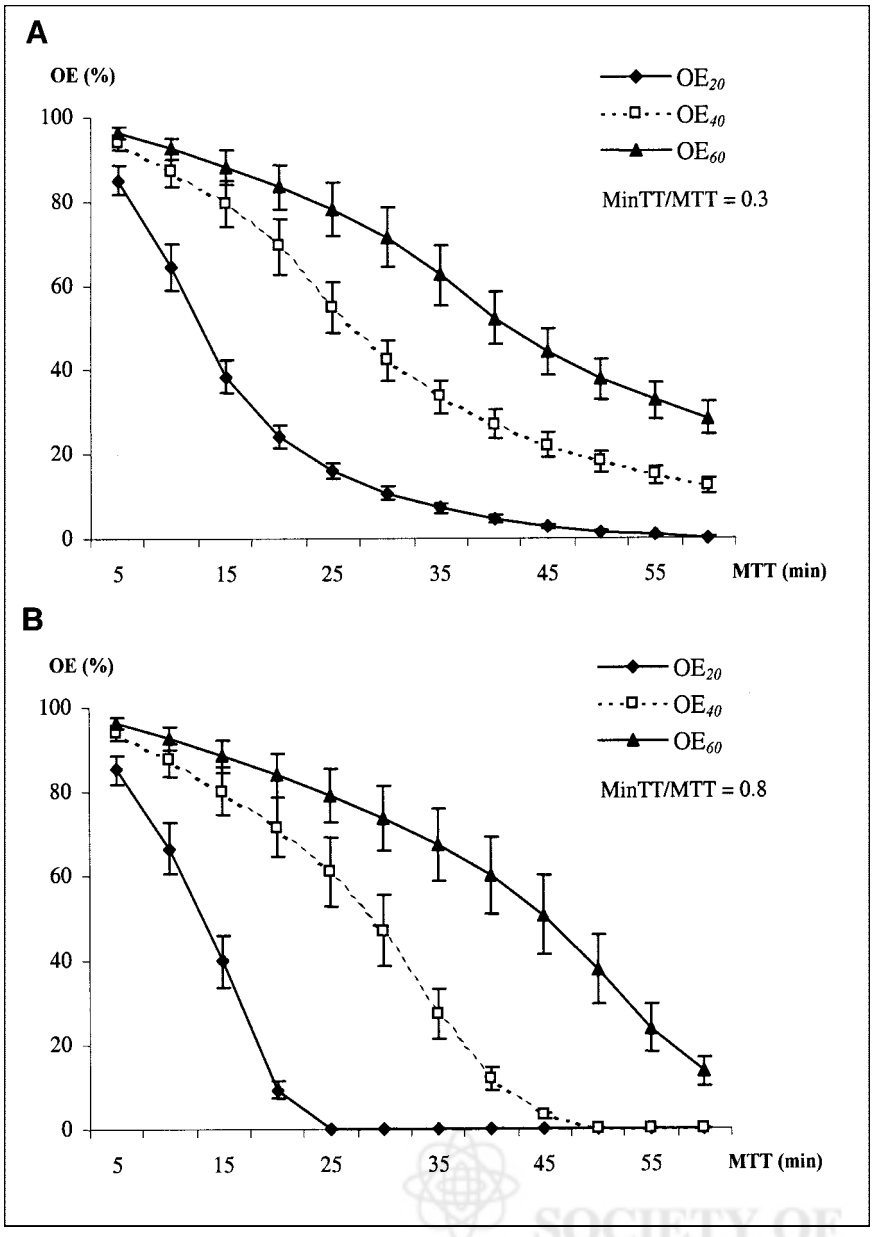

FIGURE 2. Relationship of mean of OE_t ± 1 SD to MTT for retention curves with (A) MinTT-to-MTT ratio = 0.3, and (B) MinTT-to-MTT = 0.8.

DISCUSSION

The concept of OE in the measurement of renal transit is particularly attractive. This parameter reflects the activity remaining in the kidney at a given moment compared with the total activity that has entered the kidney until that moment, and therefore indicates the efficacy of the output function. Like the deconvolution technique, OE is model-independent; unlike deconvolution, however, the stationary and linear conditions are not required for measuring OE. OE can therefore be measured at any time in the renogram, after the furosemide test, or after the postmicturition image.

According to the advocates of OE, one of its main advantages is its independence of renal clearance, rendering it superior to the classical furosemide-induced tracer washout-curve analysis. This claim has been contested by Fleming et al. (*7*). In a simulated study, these authors demonstrated the effect of renal clearance on OE. In their work, a rather unrealistic single-nephron model was used. One could therefore argue that their findings cannot be directly applied to a real-life situation (*10*).

In this study we have used a multinephron model with 2 different ratios of MinTT to MTT. Our results confirm the findings of Fleming et al. Renal clearance does influence OE and this influence is significant.

Why then the apparent disagreement between those claiming the independence of OE, and those who have observed a clear dependency on renal clearance? This may be due to confusion about which renal clearance is referred

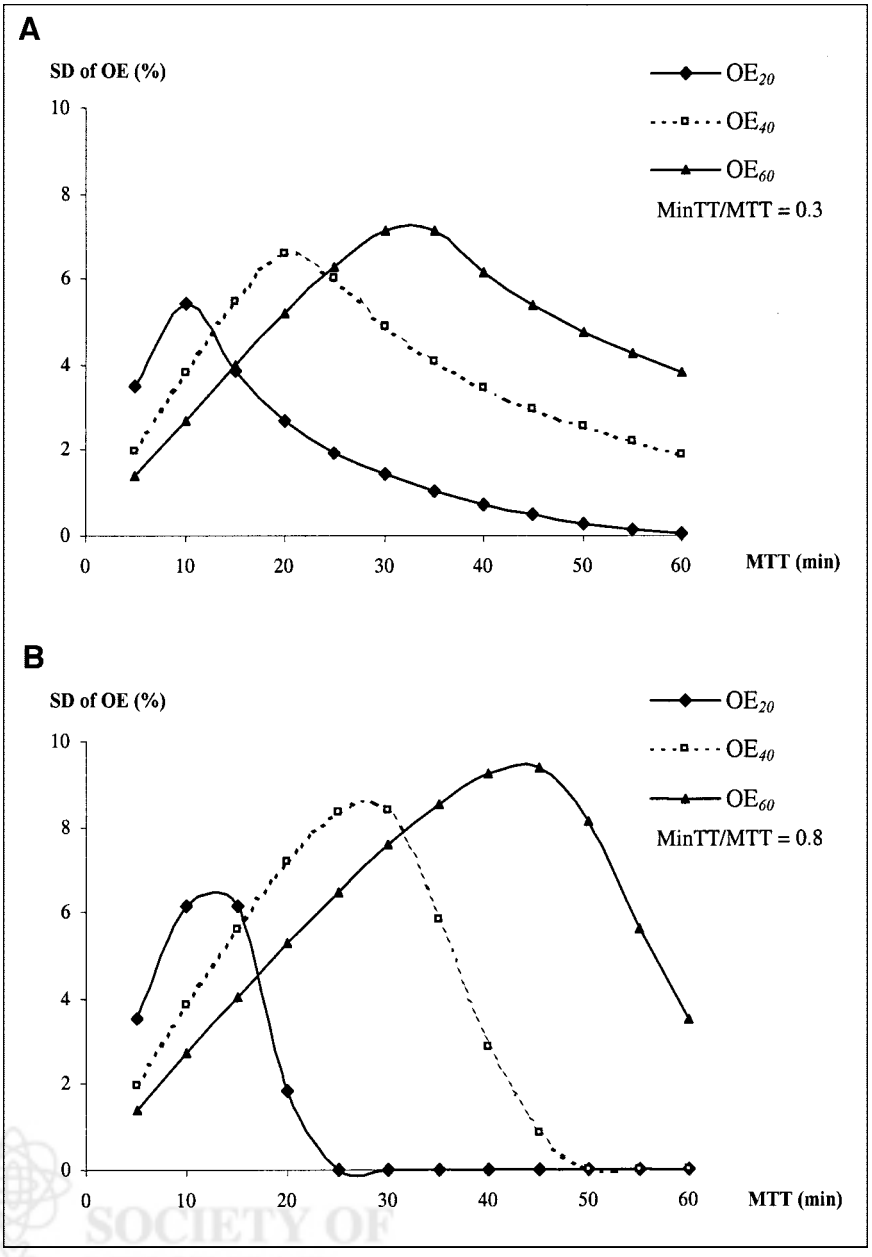

FIGURE 3. Relationship of SD of OE_t to MTT for retention curves with (A) MinTT-to-MTT ratio = 0.3, and (B) MinTT-to-MTT ratio = 0.8.

to. In a single-kidney model, OE is influenced only by the retention function, as $H(i)_m$ determines $P(i)_n$ entirely, and hence $R(i)_{n,m}$ (Eq. 2, Eq. 5). It therefore follows that, in a single-kidney model, OE can be expected to be independent of renal clearance. However, in a 2-kidney model, OE is influenced both by $H(i)_m$ and $P(i)_n$ independently, the latter being the plasma disappearance curve as the result of 2 functioning kidneys, and this in turn determines $R(i)_{n,m}$, as shown in Equation 2. The model of OE takes into account the clearance of the single kidney on which OE is determined, and is therefore independent of the function of that kidney. The clearance studied by Fleming et al., as well as by this investigation, is the overall clearance.

Although OE has been shown to be less influenced by overall clearance than more traditional parameters such as T_{max} or residual activity expressed as a percentage of maximal activity (*11*), this dependence still exists and is significant, since a change in overall clearance can produce as much as a 20% variation in OE.

CONCLUSION

According to the results of this study, renal function significantly influences OE. Taking into account the variation in OE induced by changes in overall clearance, the practical consequence of the influence of renal func-

tion is that one should take care in establishing cutoff values for obstruction, nonobstruction, and a nondiagnostic zone.

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