
How Gender and Age Affect Iodine-131-OIH and Technetium-99m-MAG3 Clearance

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Objective: The relationship between age and effective renal plasma flow (ERPF) results, as measured in nuclear medicine, is well known. This paper explores the relationships among gender, age, and ERPF measurements. After reading this paper, the nuclear medicine technologist should be able to: (a) discuss the importance of establishing normal range values for ERPF that include age and gender variables; (b) state how age affects ERPF results; and (c) state how gender affects ERPF results.

Key Words: renal function; effective renal plasma flow measurement; technetium-99m-MAG3; iodine-131-ortho-iodohippurate; age effects; gender effects

J Nucl Med Technol 2000; 28:156–158

The blood clearance of ^{99m}Tc -MAG3 correlates with ^{131}I -ortho-iodohippurate (^{131}I -OIH or hippuran) and can be used as an independent measure of renal function. The main difference is that ^{99m}Tc -MAG3 is more highly protein bound and, therefore, a smaller component is excreted by glomerular filtration. Technetium-99m-MAG3 appears to share the same transport system in the proximal tubule as ortho-iodohippurate, or hippuran (1,2). Tauxe has popularized the use of a regression equation to determine the clearance of ^{131}I -OIH based on a single plasma sample (3). The same equation can be modified for evaluating ^{99m}Tc -MAG3 clearance (4,5).

It is well established that the glomerular filtration rate and effective renal plasma flow (ERPF) in adults are age and gender dependent (6). Almost all of the available data are based on inulin and PAH clearances (7). Since ^{99m}Tc -MAG3 is almost a pure tubular agent, it provides a unique opportunity to examine changes in proximal tubular function with age and gender differences.

MATERIALS AND METHODS

Ninety-seven normal subjects, aged 27–72 y with a mean age of 51.5 y, (40 men, aged 27–71 y with mean 50.7 y, and 57 women, aged 27–72 y with mean 52.1 y), were studied to evaluate renal function and to evaluate the ERPF using a two-dimensional function derived from fitted data originally reported for hippuran (4). We excluded patients with diabetes, a history of previous renal disease, borderline hypertension, abnormal creatinine clearance, BUN, abnormal ultrasound kidney examinations, and abnormal renography. This study conformed to the rules of the Policlinico di Modena, Italy and written informed consent was obtained from all the patients for the radioisotopic examinations.

All of the patients drank 500 mL water 30 min before renographic examination. Each patient was injected with 740 kBq ^{131}I -OIH and 100 MBq ^{99m}Tc -MAG3, which were prepared in the same syringe. The gamma camera renographic study was completed and a single blood sample was drawn at 40–50 min after the injection (the optimal sample time is 44 min postinjection for the procedure to minimize the standard error of ERPF evaluation for ^{131}I -OIH).

Hippuran and MAG3 were analyzed for radiochemical purity before injection (8). The estimated percentage of free technetium in the MAG3 and of free ^{131}I in the OIH preparation was less than 4% each in all preparations.

The radioactivity of the plasma sample and a reference standard were determined in duplicate in a gamma spectrometer (ACN, Milano, Italy). A volume of 1 mL was used for both plasma samples and the reference standards (diluted 1:1000). The counting time was adjusted to obtain a maximum standard error of 1%. The samples were counted 24 h after the beginning of the procedure due to the initially high counting rates. All of the samples were corrected for decay. The results were analyzed using a computer (Macintosh PowerBook 185C, Apple with StatView II program, Apple Computer Inc., Cupertino, CA; Abacus Concept SAS Institute, Cary, NC) and an IBM DOS-based program, called Stat Calc (version 1, SPSS, Chicago, IL). The clearance was calculated using the modified Tauxe formula to take into account the time the sample was withdrawn. Using

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the following formula, the useful time of blood sampling varies from 35–50 min after radioisotope injection:

$$\text{ERPF}(\text{mL}/\text{min}) = F_{\max}(1 - e^{-\alpha(\text{dose}/V_T - V_{\text{lag}})})$$

where:

$$F_{\max} = 1553.231 - 35.490T + 0.833T^2 - 0.00567T^3$$

$$\alpha = 0.025 - 0.0004535T - .0000002204T^2 + 0.00000003349T$$

$$V_{\text{lag}} = 4.672 + 0.261T - 0.004323T^2,$$

T = sampling time

Dose/ V_T = cps/L of plasma at time T.

The modifications of the Tauxe formula (4) are described by F_{\max} , V_{lag} , and α , which are evaluated using a polynomial fitting (3° or 2°) obtained from the data published by Tauxe in the original paper. Samples were analyzed for statistical significance using paired *t* tests. A *P* value of 0.05 was taken as the lower limit of statistical significance.

RESULTS

There was correlation between the estimated clearance of ^{131}I -hippuran and $^{99\text{m}}\text{Tc}$ -MAG3 independent of gender (Fig. 1) (BS is body surface area):

$$\text{Clearance OIH/BS (ml/min)} = -3.69 \times \text{AGE} + 474$$

$$r = 0.51 \quad p < 0.001$$

$$\text{Clearance MAG3/BS (ml/min)} = -2.20 \times \text{AGE} + 266$$

$$r = 0.53 \quad p < 0.0001$$

A comparison of the slopes of the linear fits using the Student *t* test for MAG3 clearance and OIH versus age yields a *t* value of 2.79, where $P < 0.001$. We also evaluated the relationship

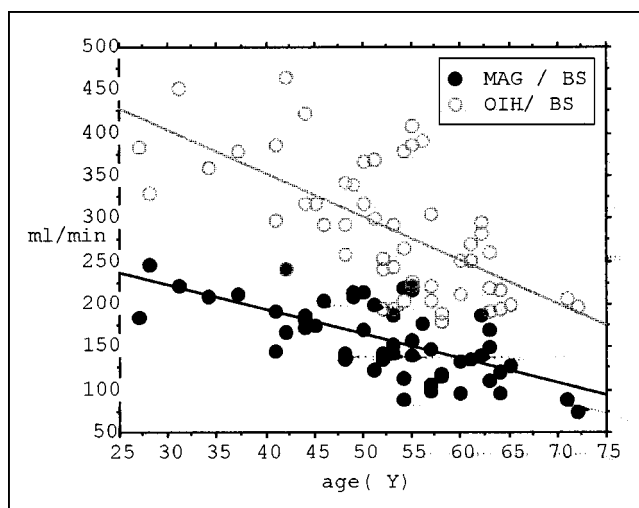


FIGURE 2. Clearance of $^{99\text{m}}\text{Tc}$ -MAG3 and ^{131}I -OIH versus age in women. BS is body surface area (evaluated from Du Bois' formula).

between MAG3 clearance, hippuran clearance, and patient age and gender (Figs. 2 and 3).

Among the women the relationship between age and clearance was:

$$\text{Clearance OIH} = -5.078 \times \text{AGE} + 555$$

$$r = 0.64 \quad p < 0.0001$$

$$\text{Clearance MAG3} = -2.854 \times \text{AGE} + 308$$

$$r = 0.65 \quad p < 0.0001$$

Among the men the relationship between age and clearance was:

$$\text{Clearance OIH} = -2.48 \times \text{AGE} + 395$$

$$r = 0.39 \quad p < 0.02$$

$$\text{Clearance MAG3} = -1.58 \times \text{AGE} + 223$$

$$r = 0.433 \quad p < 0.005.$$

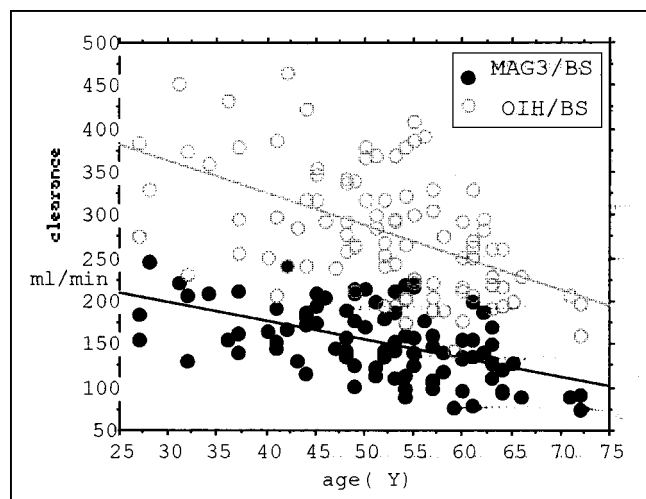


FIGURE 1. Technetium-99m-MAG3 and ^{131}I -OIH clearance versus age in 97 normal patients.

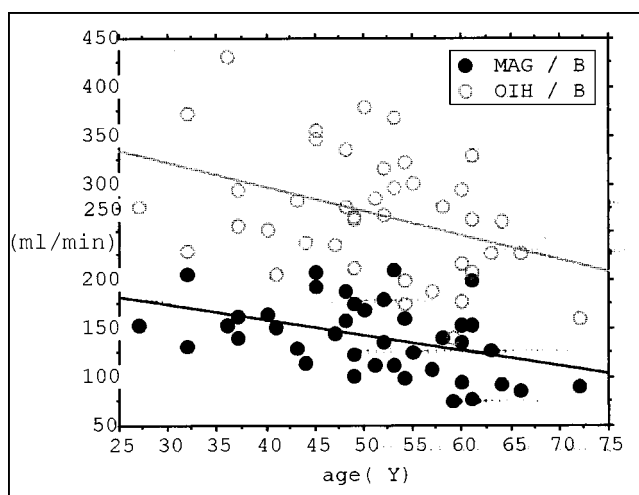


FIGURE 3. Clearance of $^{99\text{m}}\text{Tc}$ -MAG3 and ^{131}I -OIH versus age in men. B is body surface area (evaluated from Du Bois' formula).

DISCUSSION

The values of OIH and MAG3 clearance, normalized to body surface, appear to be age-dependent. The percentages of the clearance decrement evaluated from the linear fits for MAG3 and OIH were 59% and 54%, respectively, from 27–72 y of age. These data are comparable to earlier studies using PAH (6). These results confirm that age needs to be taken into account when evaluating the clearance results of ^{131}I -hippuran and $^{99\text{m}}\text{Tc}$ -MAG3 for valid reference values.

Previous studies used primarily PAH or inulin (6,7). Watkin (6) reported a relationship between PAH clearance and age of 820 mL/min ($6.75 \times \text{age}$). Similar relationships have been noted by Brod (9) and by Wessen, who compiled the existing data in 1969 (10). Technetium-99m-MAG3 clearance provides an estimate of tubular extraction.

The differences in the regression equations for hippuran and MAG3 with age and gender could suggest differences between tubular and glomerular function, with respect to these parameters. Our data suggest that there is a decline in renal function that occurs with age.

CONCLUSION

A normal man might be expected to have a clearance at age 60 that is only 58% of that of a 20-y-old, as measured by MAG3. A woman at age 60 might have a value that is 57% of a 20-y-old. This is an important consideration in comparing clearances in

individuals of different ages and in determining normal range values.

MAG3 is almost entirely secreted by the proximal tubule. These data suggest that proximal tubular function and glomerular function decline with age at a similar rate.

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