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EFFECT OF AGE AND SEX ON GLOMERULAR FILTRATION RATE MEASURED BY ^{51}Cr-EDTA

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1. The effect of age and sex on glomerular filtration rate (GFR) was measured by the ^{51}Cr-EDTA radioisotopic method in 76 normal individuals (43 women and 33 men).

2. Age has a significant effect on GFR. Subjects aged 41 to 60 years have GFR values [104.5 ± 16.5 ml min^{-1} (1.73 m^2)$^{-1}$, N = 43] lower than younger individuals aged 20 to 40 years [116.6 ± 11.2 ml min^{-1} (1.73 m^2)$^{-1}$, N = 33]. GFR decreases after 40 years of age by approximately 6.0 ml min^{-1} (1.73 m^2)$^{-1}$ per decade.

3. GFR values in women [105.9 ± 16.0 ml min^{-1} (1.73 m^2)$^{-1}$, N = 43] were lower when compared to men [114.8 ± 14.3 ml min^{-1} (1.73 m^2)$^{-1}$, N = 33].

4. We conclude that the effect of sex and age must be taken into account when establishing reference values for GFR.

Key words: glomerular filtration rate, age, sex.

Introduction

Accurate measurement of glomerular filtration rate (GFR) is essential for the early diagnosis and follow-up of patients with renal disease or after kidney transplantation. In order to correctly interpret changes in GFR due to renal diseases the effect of sex and age should be taken in account. The influence of age on GFR has been clearly established and several studies have demonstrated a decrease in renal function particularly after 40 or 50 years of age (Davies and Shock, 1950; Rowe et al., 1976; Slack and Wilson, 1976; Granerus and Aurell, 1981; Morrison et al., 1983). However, there are few but contradictory data about the effect of sex on GFR in human subjects. It is commonly believed that men normally have a slightly higher GFR than women (Wesson, 1969), although some investigators (Slack and Wilson, 1976; Granerus and Aurell, 1981) did not observe sex differences.

The objective of the present study was to determine the influence of sex and age on GFR measured by the single ^{51}Cr-EDTA injection technique in men and women aged 20 to 60 years.

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Subjects and Methods

Subjects

Seventy-six healthy volunteers (43 females and 33 males), with a body mass index <30 kg/m² and not on drug treatment were studied. These individuals did not have a family history of diabetes mellitus, were normotensive according to WHO criteria and did not present abnormalities in routine biochemical tests. The age range was 20 to 60 years, and females and males were grouped at 10-year intervals. Informed consent was obtained from each individual. The study protocol was approved by the Ethics Committee of the Hospital.

Glomerular filtration rate

The procedure was performed at 8:00 a.m. after an overnight fast. GFR was measured by the technique described by Chantler and Barratt (1972). A single bolus of 5.55 MBq ^{51}Cr-EDTA (Instituto de Pesquisas Energéticas e Nucleares, São Paulo, Brazil) was injected into the cubital vein on the forearm and blood samples were taken from the opposite arm 2, 3 and 4 h later for measurement in a gamma-counter. The activity of each sample (in log cpm) was plotted against time and a monoexponential line fitted by linear regression. This allows a microcomputer calculation of GFR which was corrected to 1.73 m² body surface area.

For four subjects, GFR measurement was repeated on three additional occasions in order to obtain the mean intra-individual coefficient of variation.

Statistical analysis

Parametric tests were used because the GFR values presented a normal distribution. The results were expressed as mean ± SD. GFR data were analyzed by two-way ANOVA, taking into consideration 2 factors, i.e., sex and age. The independent effect of age on GFR was analyzed by one-way ANOVA and the differences between the age groups were further analyzed by the multiple comparison test (Student-Newman-Keuls test). Differences in GFR between sexes were analyzed by the F test. The level of significance for statistical analysis was set at $P<0.05$.

Results

The GFR values for men and women of different ages are presented in Table 1 and Figure 1. The mean intra-individual coefficient of variation was 12%. Age had a significant effect on GFR ($F = 4.4749$, $P = 0.0061$), and the multiple comparison test demonstrated that the GFR values for subjects aged 50 to 60 years were significantly lower ($P<0.05$) than those for individuals aged 20 to 30 and 31 to 40 years. There was no difference between subjects aged 20 to 30 and 31 to 40 years and between subjects aged 31 to 40 and 51 to 60 years. The GFR values of subjects aged 41 to 50 years were not different from those for the other groups, but since there was a clear trend to reduction in this group and the values observed were quite similar to those of the subjects aged 51 to 60 years, it was arbitrarily decided to select two age subgroups: 20 to 40 and 41 to 60 years. The GFR of the younger individuals was higher than that of the older group (116.6 ± 11.2 ml min^{-1} (1.73 m²)$^{-1}$ *vs* 104.5 ± 16.5 ml min^{-1} (1.73 m²)$^{-1}$, $P = 0.001$). This means that GFR decreases after 40 years of age, in both men and women, by approximately 6.0 ml min^{-1} (1.73 m²)$^{-1}$ per decade.

Table 1 - *Effect of age and sex on glomerular filtration rate of normal individuals measured by the ^{51}Cr-EDTA single-injection method.*

Data are reported as means ± SD in ml min^{-1} (1.73 m²)$^{-1}$ for the number of normal individuals given in parentheses. *P<0.05 compared to ages 20-30 and 31-40 (ANOVA, Student-Neuman-Keuls test).

Sex	Age (years)			
	20-30	31-40	41-50	51-60
Men	114.8 ± 11.1 (10)	123.4 ± 12.3 (6)	113.9 ± 15.6 (8)	109.7 ± 16.9* (9)
Women	115.8 ± 14.0 (8)	114.7 ± 11.0 (9)	101.5 ± 15.8 (12)	98.3 ± 15.5* (14)

In the group as a whole, the GFR was lower in women when compared to men (105.9 ± 16.0 ml min^{-1} (1.73 m²)$^{-1}$ *vs* 114.8 ± 14.3 ml min^{-1} (1.73 m²)$^{-1}$, $P = 0.014$). This difference was more evident after 30 years of age, although comparison of the GFR of men and women in the four age sub-groups taken individually did not achieve statistical significance. In the two-way ANOVA, age group and sex did not interact ($F = 0.841$, $P = 0.47$), thus confirming their independent effects on GFR.

A simplified table for reference values of ^{51}Cr-EDTA GFR constructed from these data for routine clinical use is presented in Table 2.

Table 2 - *Simplified normal reference values for glomerular filtration rate measured by the single ^{51}Cr-EDTA injection technique.*

Data are reported as means ± SD in ml min^{-1} (1.73 m²)$^{-1}$ for the number of normal individuals given in parentheses. Data taken from Table 1. *P<0.05 compared to ages 20-40 (Student *t*-test).

Sex	Age (years)	
	20-40	41-60
Men	118.0 ± 12.0 (16)	111.7 ± 16.0* (17)
Women	115.2 ± 12.1 (17)	99.8 ± 15.4* (26)

Discussion

The effect of age on GFR was confirmed in the present study. A reduction rate of 6 ml/min per decade observed after 40 years of age is in agreement with a previously reported rate of around 4 ml/min per decade before 50 years and of 10 ml/min per decade thereafter (Granerus and Aurell, 1981). Davies and Shock (1950) using inulin clearance in 70 males aged 24 to 89 years, observed that the GFR of men 80 to 90 years of age is approximately half of that of men 20 to 30 years old. This reduction was also more evident after 50 years of age. On the other hand, Slack and

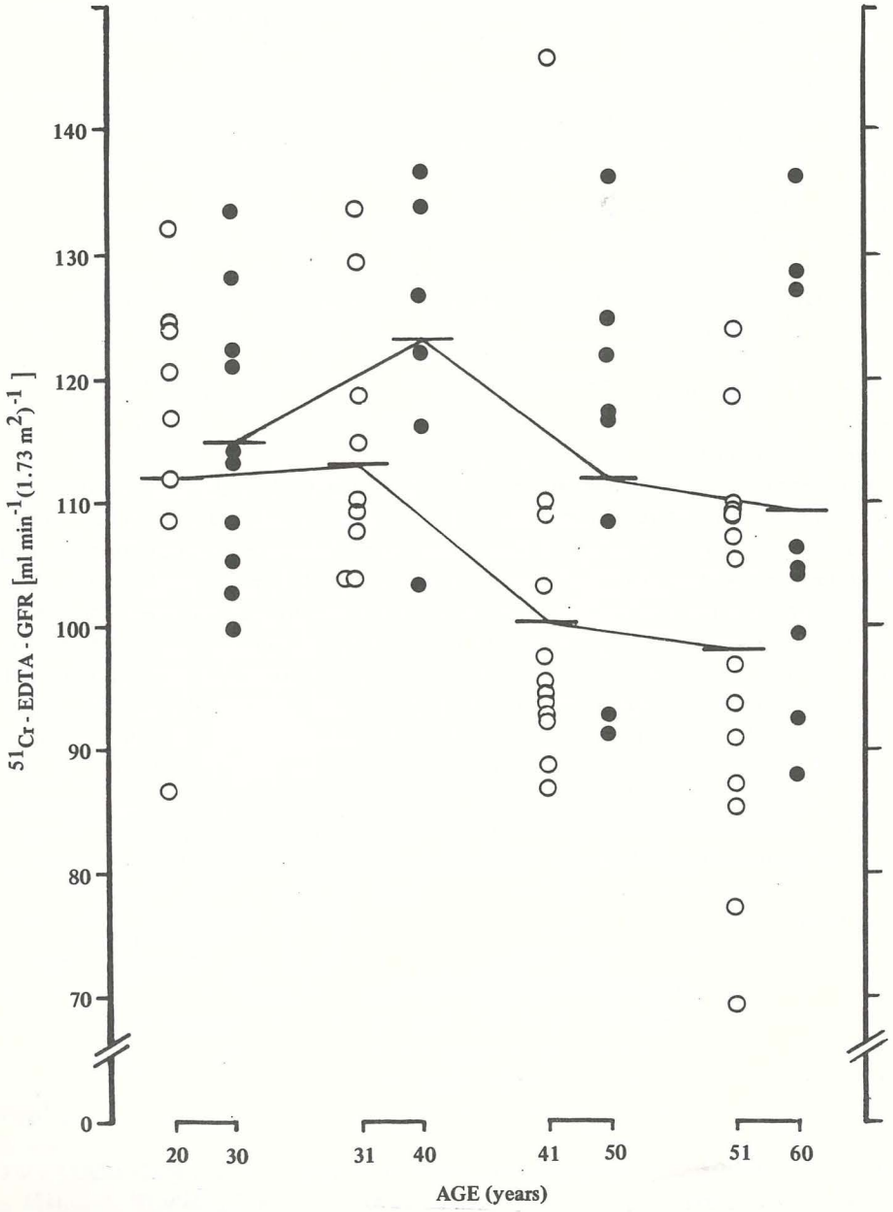

Figure 1 - Distribution of glomerular filtration rates as a function of age and sex of normal subjects. GFR was determined by the ^{51}Cr-EDTA single-injection method. Data are reported for women (●, N = 43) and men (○, N = 33) for the age groups given on the abscissa. The lines connect the mean values for each group.

Wilson (1976), studying 141 healthy renal transplant donors, observed a linear age-related decline in inulin clearance of 4 ml/min per decade beginning in the 20's. These authors were unable to demonstrate a remarkable fall in renal function in the 40- to 60-year age group. The decline in GFR may be related to several physiologic and pathologic changes seen in the aging kidney. A progressive reduction in renal plasma flow occurs simultaneously with the decrease in GFR (Slack and Wilson, 1976). Factors contributing to this decreased renal plasma flow include an age-related decline in cardiac output and reductions in the renal vascular bed (Rowe et al., 1976). The elastic layers of small arteries becomes thicker and reduplicated, encroaching on the lumen and the average size of nephrons diminishes (Morrison et al., 1983). Furthermore, Kaplan et al. (1975) observed a substantial increase in the number of sclerotic glomeruli after the age of 50.

The effect of sex on GFR is still unsettled. The observed results revealed a 10% decrease in women's GFR values when compared with men's values. These data are in accordance with series reported by Wesson (1969). This investigator summarized the data combined from different laboratories supporting the view that GFR measured by inulin clearance is significantly higher in men than in women at any age. Experimental studies in Munich-Wistar rats also confirmed a sex difference in GFR (Munger and Baylis, 1988; Remuzzi et al., 1988). The lower GFR values observed in female rats are due to a greater vascular resistance in females than in males probably related to the effect of ovarian hormones on renal hemodynamics (Munger and Baylis, 1988). However, a sex effect on the GFR of human beings has not been confirmed by others. Slack and Wilson (1976), studying GFR measured by inulin clearance, did not observe any sex difference. Landahl et al. (1981) also did not observe differences in GFR measured by ^{51}Cr-EDTA between 40 men and 32 women 70 to 75 years old.

In conclusion, the present data confirm that GFR decreases with age and that the women's values are lower than men's. These factors must be taken in account when establishing reference values.

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