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ANNUAL CHANGE OF ESTIMATED GLOMERULAR FILTRATION RATE IN HEALTHY INDIVIDUALS

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Abstract

Physiologically, GFR level should be stable up to the end of the fifth decade of life. When measured more frequently, wide dispersion of GFR results have been seen, but, after 5th decade GFR is expected to reduce by 1ml/min/1,73m2 yearly. The aim of this study was to calculate the change of estimated GFR on annual level and its correlations in healthy individuals.

This was a retrospective observational study on 62 healthy subjects during 6 years. Demographical characteristics as gender, age, BMI, obesity (defined as BMI above 30kg/m^2) and annual creatinine were obtained from medical files at the general practitioner. Serum creatinine level was measured at one biochemical laboratory. eGFR was calculated with CKD EPI formula. Calculation of the mean annual GFR change (δGFR) was done through the method of data smoothing. Statistics: Continuous variables are shown as average and standard deviation and the nominal ones with number and percent. GFR change was correlated with age and BMI. Comparative analyses of δGFR in relation to gender and obesity was done by non-parametric Mann-Whiney U test. P was considered significant if less than 0.05.

Mean age of the study group was 39.5 years, dominantly male (78%). Mean BMI was 26,3 ± 3.81 kg/m^2, 13% were obese. The mean annual GFR fluctuated (101.8 ± 5.56; 108.0 ± 31.04; 102.8 ± 18.28;103.2 ± 20.49; 99.10 ± 24.28; 103.55 ± 20.74 mL/min/1.73m^2, respectively). The δGFR median value was 2.3 mL/min/1.73m^2 with range of -23 to +20, and its correlations with age and BMI were insignificant (r= -0.058, p=0.681, r= 0.128, p=0.111, respectively). The δGFR did not differ significantly between genders and obese vs nonobese subjects (p=0.577; p=0.768, respectively).

This study demonstrated that annual GFR change wasn't correlated to age, gender and BMI. It also elucidated the fact of a high variable eGFR levels and its annual decline in presumed healthy persons. This fact emphasizes the need for thorough evaluation of the candidates for kidney donors, especially when applying the expanded criteria.

Key words**:** GFR, healthy subjects, kidney function decline, donors.

Introduction

When estimating kidney function in health or disease, GFR is commonly used as the adequate indicator in the clinical settings. Apart of the golden standard for a measured GFR, estimated (eGFR) encountering serum creatinine, is preferably chosen for ordinary practise and basic assessments [1].

In the evaluation process of a kidney donor candidate, wide spectrum of tests is obtained, but before measuring GFR, donors' evaluation starts with eGFR calculation[2].

Persons with eGFR below 60ml/min/1.73m^2 are declined for donors. Physiologically, GFR level should be stable up to the end of the fifth decade of life. When measured more frequently, wide dispersion of GFR results have been seen, with daily variations depending on different factors [3].

These biological fluctuations or biased results could interfere the process of kidney donation. Shortage of organs is the reason that in some programs for living kidney donation, as expanded criteria donors, those with advanced age, well controlled hypertension, diabetes and obesity are being excepted [4,5].

Different studies have demonstrated the start of kidney function in the fourth decade but generally it is accepted that after the 5th decade of life GFR is expected to reduce by 1ml/min/1,73m2 yearly [6,7].

The aim of this study was to calculate the change of estimated GFR on annual level and its correlations in healthy individuals.

Material and methods

This was a retrospective observational study on 62 healthy subjects during 6 years. Demographical characteristics as gender, age, BMI, obesity (defined as BMI above 30kg/m^2) and annual creatinine were obtained from medical files at the general practitioner. eGFR was calculated with CKD EPI formula. Serum creatinine level was measured at one biochemical laboratory.

Calculation of the mean annual GFR change (δGFR) was done through the method of data smoothing (average of all previous minus next eGFR value), considering positive values of δGFR as per decline of eGFR in ml/min/1.73m^2.

Statistics: Continuous variables are shown as mean and standard deviation and the nominal ones with number and percent. eGFR change was correlated with age and BMI with Pearsons test.

Comparative analyses of δGFR in relation to gender and obesity was done by non-parametric Mann-Whiney U test. P was considered significant if less than 0.05.

Results

Baseline demographic, anthropometric and biochemical parameters at baseline are shown in Table 1. The mean age of subjects was 39.5 years in range from 29 to 52 years and dominantly were men (78%). The BMI ranged from 19 to 40 and 13% of all were obese with BMI over 30Kg/m^2. The creatinine level was in referent range and mean value of 101.8 ± 5.56 mL/min/1.73m^2.

Table 1. Baseline demographic, anthropometric and biochemical parameters

N=63	Mean ± SD N^o (%)	Range Min-Max
Age (years)	39.5 ± 5.56	**29 - 52**
Gender (male)	49 (78%)	
BMI (Kg/m^2)	26.3 ± 3.81	19 – 40
BMI>30 (Kg/m^2)	8 (13%)	
Creatinine (μmol/L)	71.65 ± 14.59	54 - 107
(baseline) eGFR (mL/min/1.73m^2)	101.8 ± 5.56	66 - 130

The mean annual eGFR changed through the next five years (108.00 ± 31.04; 102.80 ± 18.28; 103.21 ± 20.49; 99.10 ± 24.28; 103.55 ± 20.74 mL/min/1.73m^2, respectively). The fluctuations are presented graphically in Figure 1. All eGFR values remained in referent range.

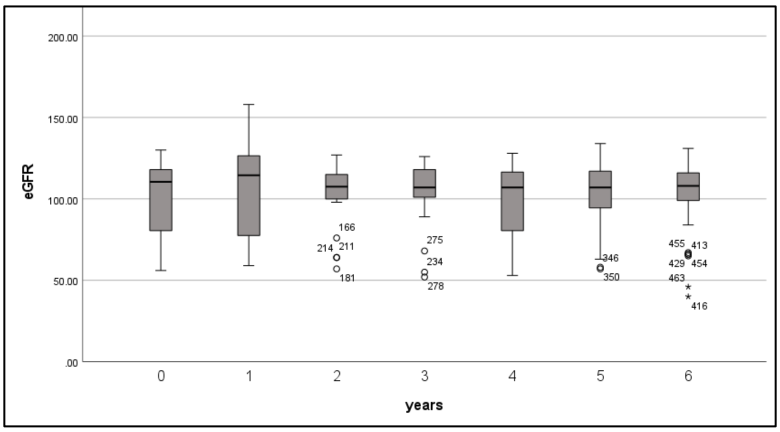

Figure 1. Box-plot of annual eGFR from baseline to sixth year of follow up.

The average annual change of eGFR showed wide range between -23 up to 20 mL/min/1.73m^2, with mean level of 2.41 ± 7.36 mL/min/1.73m^2 and median of 2.30 mL/min/1.73m^2. Out of all, 26 (40%) of subjects presented with δGFR above median. The distribution of δGFR and its bell-shaped curve is shown in Figure 2.

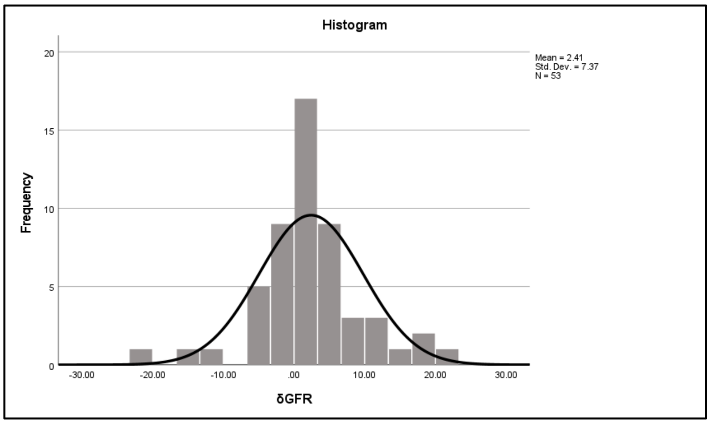

Figure 2. Distribution of the annual change of renal function – δGFR in mL/min/1.73m^2

The correlation analysis between age and BMI with the annual δGFR showed no significant association, (r= -0.058, p=0.681; r= 0.128, p=0.111, respectively), as presented in Figure 3.

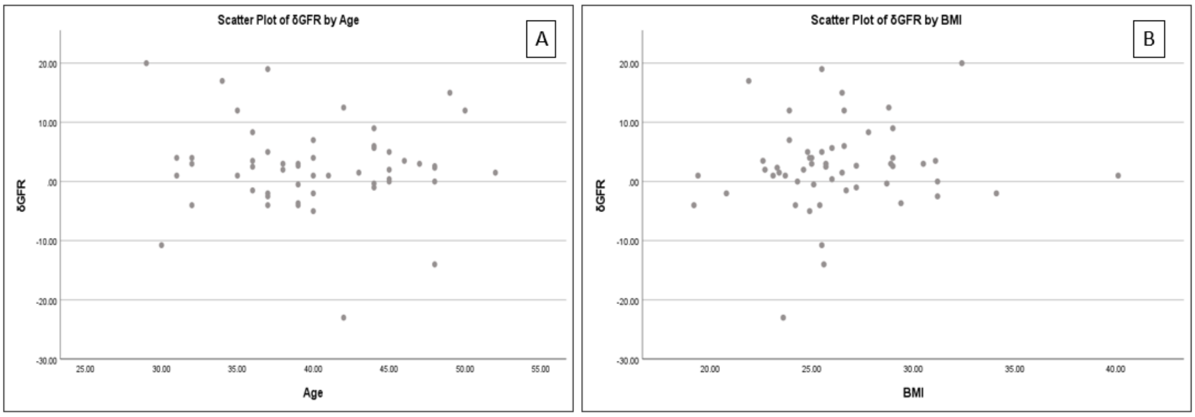

Figure 3. Correlation between age (A) and BMI (B) with annual change of eGFR

The subjects with annual decline of eGFR over median of δGFR(2.3ml/min/1.73m^2) weren't different in respect of BMI as well (Figure 4). Mann-Whitney test declared no difference in δGFR in respect of the gender and obesity (p=0.577; p=0.768), respectively.

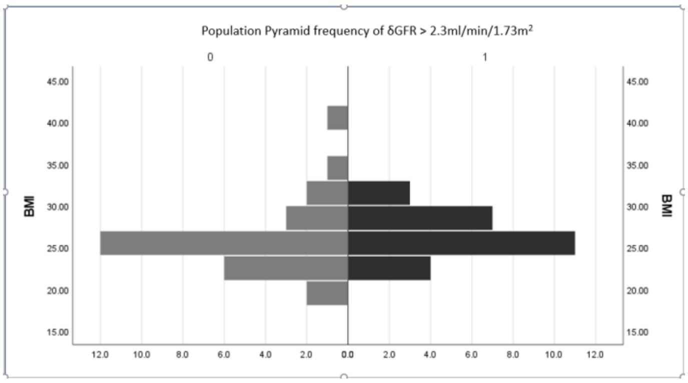

Figure 4. Distribution of subjects BMI in respect of median level of δGFR.

Discussion

Our study analysed a group of young healthy subjects of age between 29 – 52 years, with a wide diapason of values in serum creatinine, as well in eGFR (66-130ml/min/1.73m^2). The annual intra-individual variations of creatinine and eGFR were rather high as were in Lees population study [3].

The eGFR remained in reference values though the 6 years of follow up as shown in previous studies for same aged populations [1]. Conversely, we have found a median of 2.3 ml/min/1/73m2 for kidney function decline, in spite of those subjects being under 50 years of age. In a large Japanese study on 290268 healthy 40 years old subjects with follow up of ten years, the annual kidney function decline was 0.36 ml/min/1/73m^2, but for the patients with proteinuria the decline was steeper, tripling the figures [8].

Halve portion of our healthy subjects presented with decline of the kidney function.

As possible explanation we find the lack of information on proteinuria. The obesity has been recognized as a risk factor of CKD [9].

In our study 13% of subject had BMI over 30 Kg/m^2, but we failed to associate this condition with the annual decline of eGFR.

Our study has several limitations. In addition to the lack of information on data about proteinuria and smoking, the major concern is in respect of the small number of healthy subjects, and the power of the study.

Conclusion

This study demonstrated that annual GFR change wasn't correlated to age, gender and BMI in healthy subjects. It elucidated the fact of a high variable eGFR levels and its annual decline in presumed healthy persons. This fact emphasizes the need for thorough evaluation of the candidates for kidney donors, especially when applying the expanded criteria.

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