New normal values not related to age and sex, of glomerular filtration rate by ^{99m}Tc-DTPA renal dynamic imaging, for the evaluation of living kidney graft donors

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Abstract

The aim of this study was to investigate the normal values of glomerular filtration rate (GFR) by technetium-99m diaethylene triamine pentaacetic acid (^{99m}Tc-DTPA) renal dynamic imaging for living kidney graft donors. *In a total of 212 candidate donors*, GFR was examined using ^{99m}Tc-DTPA renal dynamic imaging. Donors with GFR≥80mL/(min·1.73m^2) and as low as with GFR≥70mL/(min·1.73m^2) but a normal endogenous creatinine clearance rate (CCr) were qualified for living kidney donation. Differences in GFR level based on sex and age were analyzed using rank correlation coefficient. Out of the 212 candidates, 161 were finally selected as kidney graft donors. *The double kidney total GFR* between the male and female donor groups, the GFR levels among differently-aged donor groups, and the GFR levels between the elderly (>55 years) and young- and middle-aged (≤55 years) donor groups did not show any significant difference (P>0.05). After kidney donation, renal function measured by blood urea nitrogen (BUN) and serum creatinine of all donors returned to normal within one week, and no serious complications were noticed. *In conclusion*, renal dynamic imaging by ^{99m}Tc-DTPA had a good accuracy and repeatability in GFR evaluation for living kidney donors. Candidate donors with GFR between 70mL/(min·1.73m^2) and 80mL/(min·1.73m^2) can be selected as kidney donors after strict screening. In living kidney donors, GFR is not significantly correlated with age or sex.

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Introduction

Kidney transplantation is nowadays one of the most preferred treatment methods for end-stage renal diseases, but the shortage of donated organs greatly restricts the development of this treatment. Living donors kidney transplantation possesses the virtues of sufficient pre-operative set-up time, of short warm ischemia time, so as to avoid rejection reactions and of improving the long-term survival rate of the transplanted kidneys. Accurately evaluating the glomerular filtration rate (GFR) in a living kidney transplantation donor, is of great importance to guarantee the post-operative well being of both the donor and the recipient [1-3]. Among different GFR detection methods, inulin clearance has been widely accepted as the gold standard. Chromium-51-ethylenediaminetetraacetic acid (^{51}Cr-EDTA) can be filtrated freely by glomeruli, and it has a plasma clearance close to inulin clearance. Therefore, ^{51}Cr-EDTA clearance was previously used for GFR determination. Later on, scholars found that technetium-99m diaethylentriaminopentaacetic acid (^{99m}Tc-DTPA) can almost be completely filtrated by glomeruli rather than reabsorbed or excreted by kidney tubules; its renal or plasma clearance is highly consistent with inulin clearance, for which its clearance can accurately reflect GFR and therefore can replace inulin clearance as the gold standard for scientific research; compared with ^{51}Cr-EDTA, it has a lower radiologic dose and is more economical; furthermore, renal dynamic imaging can be performed in the meantime, for which ^{99m}Tc-DTPA has been extensively used as a routine imaging agent in clinic. Furthermore, the ^{51}Cr-EDTA method is complicated and costly and its application in routine is greatly restricted. By contrast, ^{99m}Tc-DTPA renal dynamic imaging is rather easy to operate, safe, noninvasive and directly studies the GFR values of both kidneys and urinary flow accurately and repeatedly. These advantages make ^{99m}Tc-DTPA renal dynamic imaging widely applied and accepted in clinical practice [4-7]. Although ^{99m}Tc-DTPA renal dynamic imaging has been used for kidney donors' GFR evaluation in most Chinese transplantation centers, reports on the normal GFR value for donor selection, the quality control during GFR determination, and the correlations of GFR with sex and age are rare [8] and may vary in different population areas. Based on the aforementioned, in this study, clinical data of 212 kidney donor candidates were analyzed to explore the GFR normal reference value for living kidney donors, as well as the correlations of the value with age and sex.

Subjects and methods

Between October 2007 and March 2009, we conducted GFR evaluations for 212 living donors. According to the relationships of donors with recipients, 31 of 161 donors were parents, 48 were siblings, 17 were couples, 4 were children, and 61 were branch line relatives within three generations such as uncles, nephews, and cousins, and relatives' candidates for kidney graft donors using ^{99m}Tc-DTPA renal dynamic imaging. We further analyzed the donors' preoperative and postoperative follow-up data and explored the correlations of normal GFR with age and sex.

Donors' selection

All candidates received thorough examination, including liver and kidney ultrasound tests for, hepatitis viral infection, blood type and tissue matching between the donor candidate and the recipient. Those who met the general requirements as above underwent ^{99m}Tc-DTPA renal dynamic imaging for GFR determination as well as CT scanning for both kidneys vessels and urinary tract imaging. A GFR of more than 80mL/(min·1.73m^2) was considered normal. Candidates with GFR between 70mL/(min·1.73m^2) (including 70mL/(min·1.73m^2)) and 80mL/(min·1.73m^2) underwent endogenous creatinine clearance rate (CCr) determination and if CCr was normal, the candidate was considered as a normal candidate for kidney donation. Candidates with GFR <70mL/(min·1.73m^2) were considered unqualified.

^{99m}Tc-DTPA renal dynamic imaging

The single photon emission tomography (SPET) scanner in the current study was a double probe scanner (Philips, USA). Glomerular filtration rate was determined through ^{99m}Tc-DTPA renal dynamic imaging using Gates' method [9]. Diuretic administration and intravenous urography were not allowed within 3d before the detection. Within 30min before the detection, the candidate drank 500mL of tap water; his/her body height, weight and blood pressure were recorded and was asked to empty the bladder. The radioactive count rates of the injector before and after the injection were respectively measured for 1min. The imaging agent was injected into the ulnar vein in small boluses, during 21min of continuous double kidney dynamic image acquisition. The acquisition was carried out in two phases: the renal blood flow phase at 2sec/frame for 60sec and the renal function phase at 60sec/frame for 20min. The probes were equipped with low-energy general purpose collimators with an energy peak of 140keV, a window width of 20%, and a 64X64 matrix. Double kidney and background regions were delineated using the technique of regions of interest (ROI). Double kidney blood perfusion and function curves as well as the related quantitative parameters were acquired.

Grouping after donor selection

The correlations of GFR with sex and age were analyzed after donor selection. The donors were divided into two groups according to sex. Meanwhile, they were divided into four groups based on ages: the 20-29, 30-39, 40-49, and ≥50 year groups. They were further divided into the elderly (>55 years) and young- and middle-aged (≤55 years) groups. The eldest person was 62 years old.

Statistical analysis

Data were presented as mean±standard deviation ($\bar{x}$±SD) and analyzed using the SPSS 13.0 software. ANOVA was performed for comparisons among different age groups, paired or independent sample *t*-test for comparisons between groups, and rank correlation coefficient (Kendall's tau-b) for correlation analysis. P<0.05 was considered as statistically significant.

Results

GFR and donors' selection

From all subjects studied, 137 had GFR>80mL/(min·1.73m^2), 55 had GFR between 70mL/(min·1.73m^2) (including 70mL/(min·1.73m^2)) and 80mL/(min·1.73m^2) and 20 had GFR <70mL/(min·1.73m^2). Among the 55 candidates with GFR between 70mL/(min·1.73m^2) (including 70mL/(min·1.73m^2)) and 80mL/(min·1.73m^2), 29 gave up donation due to safety consideration and 26 received CCr determination, two of whom had abnormal CCr. The 24 candidates with normal CCr values included 19 males and 5 females (their CCr values were 103.8±17.4mL/(min·1.73m^2) and 99.6±15.6mL/(min·1.73m^2), respectively), they were qualified for kidney donation. Ultimately, a total of 161 out of 212 candidates were finally selected as kidney donors while the rest were excluded. Among the 161 donors, 105 were males and 56 were females. Their ages ranged from 20 years to 62 years

Table 1. *Comparison of the GFR values among differently-aged donation candidate groups ($\bar{x}$±SD)*

Group	Cases Males / Females	GFR mL/(min·1.73m^2)		
		Left kidney Males / Females	Right kidney Males / Females	Both kidneys Males / Females
20-29 years	40 12	45.6±7.2 45.0±6.6	45.0±6.0 45.0±7.8	88.8±13.2 88.8±11.4
30-39 years	27 17	45.6±7.8 44.4±7.2	46.8±7.8 46.2±7.2	91.8±15.6 91.2±13.8
40-49 years	22 16	45.6±7.2 44.4±6.0	44.4±7.8 45.0±6.0	89.4±12.6 89.4±10.8
≥ 50 years	16 11	43.2±6.6 42.6±8.4	45.6±7.8 45.6±6.6	88.8±12.6 88.2±13.8

Table 2. *Donors' GFR in different age groups ($\bar{x}$±SD)*

Age (years)	Patient (No.)	GFR (mL/(min·1.73m²))		
		LK	RK	DK
20-29	52	45.6±6.6	45.0±6.6	88.2±12
30-39	44	45.0±8.4	46.8±7.2	91.8±14.4
40-49	38	45.0±6.6	44.4±6.6	89.4±11.4
≥ 50	27	42.6±7.8	45.6±7.2	88.2±13.2

LK: left kidney; RK: right kidney; DK: both kidneys.

with a median age of 42.9±11.9 years. Their pre-donation serum creatinine (SCr) level was 61.6±9.1μmol/L. This value increased by 29.1μmol/L (47.2%, P=0.000) to 90.7±15.4μmol/L at 1 week after the donation, but was still within the normal range. Their pre-donation urea nitrogen (BUN) level was 4.3±1.0mmol/L, which increased by 0.4mmol/L (9.0%) to 4.7±1.1mmol/L at 1 week after the donation, a difference that was not significant (P=0.069). All donors were followed up for more than 8 months. Their SCr and BUN levels turned to 88.6±14.0μmol/L and 4.6±1.0mmol/L. All donors had stable renal function, and no serious complications occurred.

GFR and gender

Among the 161 donors, the left and right kidney and double kidney total GFR of the males were 45±7.8, 45.6±7.2 and 90.6±13.2mL/(min·1.73m²), and those of the females were 43.2±5.4, 44.4±7.2, and 87±10.8mL/(min·1.73m²). Comparisons between the different gender groups did not show any significant difference (P>0.05) (Table 1).

GFR and age

Different age groups (up to the age of 62 years) did not show significant differences in GFR (P>0.05). The GFR values of the elderly and young- and middle-aged groups were 88.8±13.2 and 89.4±10.2mL/(min·1.73m²), which did not show a significant difference, either (P>0.05). The results are summarized in Table 2. Correlation analyses showed that GFR was not correlated with age (r=-0.033, P=0.69; Fig. 1); the GFR values of the male and female donor groups were not correlated with age, either (r=-0.053, P=0.571; r=-0.019, P=0.754). An example of GFR clearance measurement in a subject is shown in Figure 2.

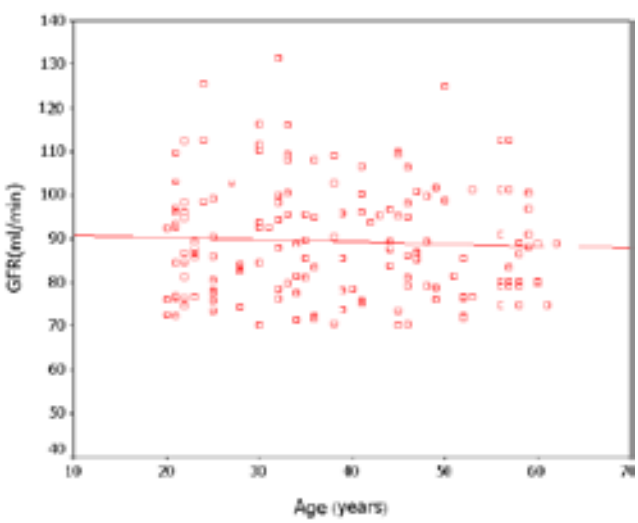

Figure 1. Change trends of the GFR values in kidneys of differently-aged donors.

Discussion

At present, the widely-adopted normal GFR value in China is >80mL/(min·1.73m²) which is based on the findings among western populations performed much earlier [10]. Recent reports have posed doubts about these values considering them too high [11, 12]. Problems with the presently-adopted normal GFR values may be: a) They were not derived from multi-centre and after large samples statistical analyses in China, especially studies of GFR in healthy kidney donors; b) They are not based on comparisons among different detection methods nor comparisons among computing methods; and c) their definition does not take into consideration possible GFR differences between eastern and western populations.

This present study did not move on to "the gold standard" detection and correlation analysis of the 20 candidates with GFR <70mL/(min·1.73m²), which may be a drawback and worth researching in the future. All donors were followed up for 8 months and their related examination indices returned to normal within a short time after they were operated. This finding indicated that donors with GFR between 70mL/(min·1.73m²) and 80mL/(min·1.73m²), have a prognosis as good as those with GFR ≥80mL/(min·1.73m²).

Based on the aforementioned results of this study as well as in related literatures [11-14], it is the opinion of the authors that a GFR value of ≥70mL/(min·1.73m²) should be considered as normal, at least, for Chinese healthy kidney donors, even though the overall renal function evaluation needs comprehensive consideration of clinical, chemical, and other imaging examinations. Post-operative follow-up data and safety assessments for large samples of kidney donors are also necessary. Multi-centre and large sample statistical analyses of different methods and long-term quantitative follow-up of GFR values after donation as well as its correlation with clinical manifestations are warranted.

Double kidney GFR values determined using Gates' method are the results of computerized automatic generation after computation of the corresponded regression

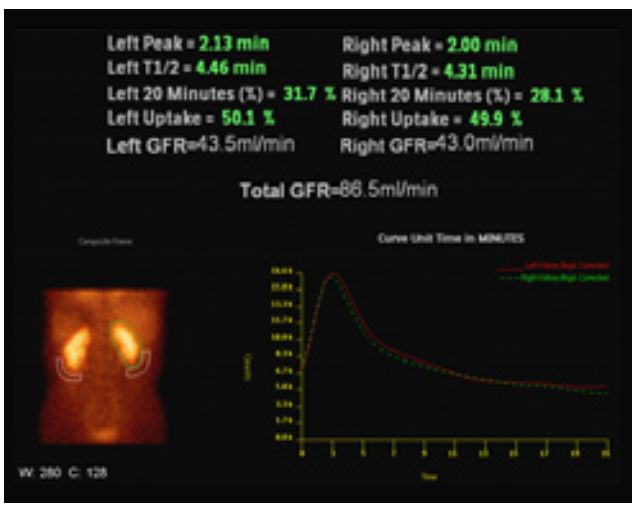

Figure 2. Example of GFR clearance measurement in a subject

equations of related variables [9]. These values can be affected by multiple factors, among which ROI selection and the method for the assessment of renal depth are important [9, 15-18]. For this reason, the suitable population and practical value of Gates' method remain controversial. Selection of ROI can directly affect the accuracy and repeatability of results. To avoid the influence caused by ROI selection, in this study, the positions of the ROI as well as their volumes were delineated strictly following Gates' method. For renal depth measurement, Gates' method makes use of the relations of renal depth to body height and weight in normal adults and then figures out the kidney position based on regression equation. In this study, all subjects were healthy adult donors, which maximally avoided the changes in kidney position caused by age or disease. Furthermore, the detection procedure in this study was performed strictly following the nuclear medicine examination procedure, which successfully avoided the influences of oedema, cardiac dysfunction, bladder overfilling, injected dose, and injection quality on the GFR values [19]. Moreover, in order to testify the repeatability of results in this study, 26 other volunteers were rechecked under the same conditions two days later, and consistent results were acquired. This further shows that the application of Gates' method in GFR determination among healthy adult donors following the exact procedure mentioning above is highly accurate and repeatable.

The correlation between GFR and age in living relative's kidney donors is another controversial topic [20-22]. Around it, three main viewpoints have been proposed: a) GFR is negatively correlated with age, b) GFR bears no correlation with age and c) GFR in male donors is negatively correlated with age while in female donors has no correlation with age. The present study showed that there was no significant difference in GFR between the young- and middle-aged and elderly groups up to the 62 years of age. This result indicated that GFR was not correlated with age, and age factor did not affect donor selection or the safety of elderly donors. This indication is consistent to what is reported in the literature [23]. Presumably, the underlying reason arises from the strict selection of living relatives for kidney transplantation donors, which almost prevents all interference in renal function from factors such as hypertension and diabetes (both hypertension and diabetes are high risk factors which can accelerate glomerulosclerosis). But this study showed that the number of elderly donors (up to the 62 years of age) was smaller, compared with the young- and middle-aged donors, which suggested that caution should be taken in the selection of more elderly donors. This study also showed that GFR in healthy kidney donors was not correlated with sex. This finding is consistent to those reported by others [24-26].

Selection of a kidney donor is primarily based on the preoperative GFR values (by ^{99m}Tc-DTPA renal dynamic imaging) and renal arteriorenal anatomic images (by multilayer CT angiography) of both kidneys. The surgeon will choose the best functioning of the kidneys of the donor for transplantation. If GFR values in both kidneys are close, the arteriorenal anatomic images will be considered, and the left kidney will be favored [27]. The kidney with a comparatively simpler arteriorenal structure will also be chosen as the donated.

It is a unique practice today to determine GFR by ^{99m}Tc-DTPA renal dynamic imaging for healthy living kidney transplantation donors' selection in transplantation centers. This test remains to be further improved in its GFR normal value selection, in handling basis of the critical value, and in correlation with other evaluation methods [28].

In conclusion, this study shows that normal values of GFR by ^{99m}Tc-DTPA renal dynamic imaging for the evaluation of living kidney graft donors were higher than or as low as 70mL/(min·1.73m^2) compared to the standing at present normal values for China. There was no age or gender difference in the normal CCr values we studied up to the age of 62 years. Renal dynamic imaging by ^{99m}Tc-DTPA had a good accuracy and repeatability in evaluating GFR for living kidney donors.

The authors declare that they have no conflicts of interest.

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Ancient Greek sayings written on main gates of USA Universities are:
a) "Always be better than others so that your ancestors shall be proud of you"
b) "Only those who have learned sciences may speak and look deep into matters"
c) "Truth is the basis of science"