Measuring or estimating GFR in potential living kidney donors

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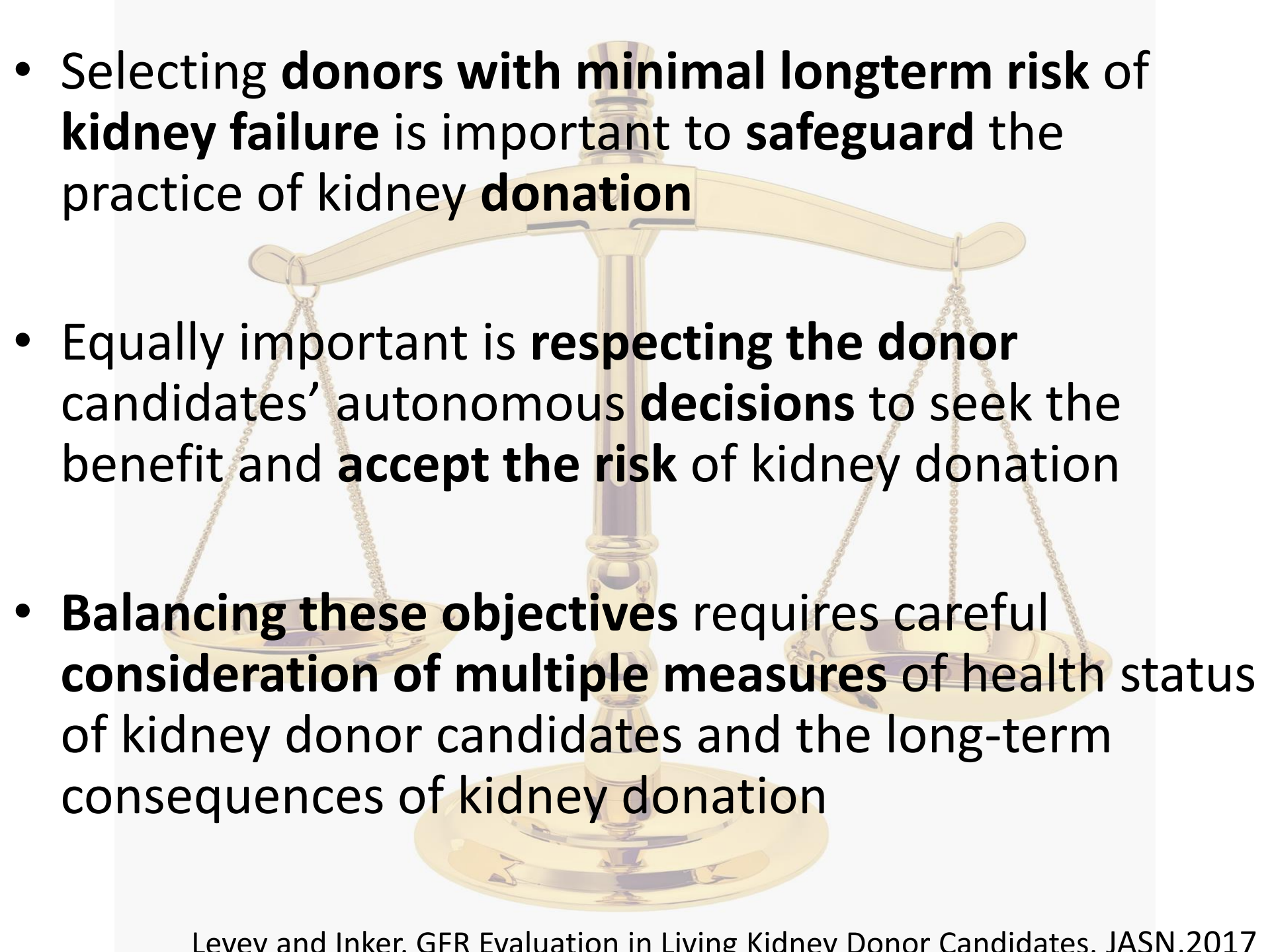
- 104 countries (90% of the worldwide population)
- around 100 800 solid organ transplants per year
- 69 400 kidney transplants (46% from living donors)

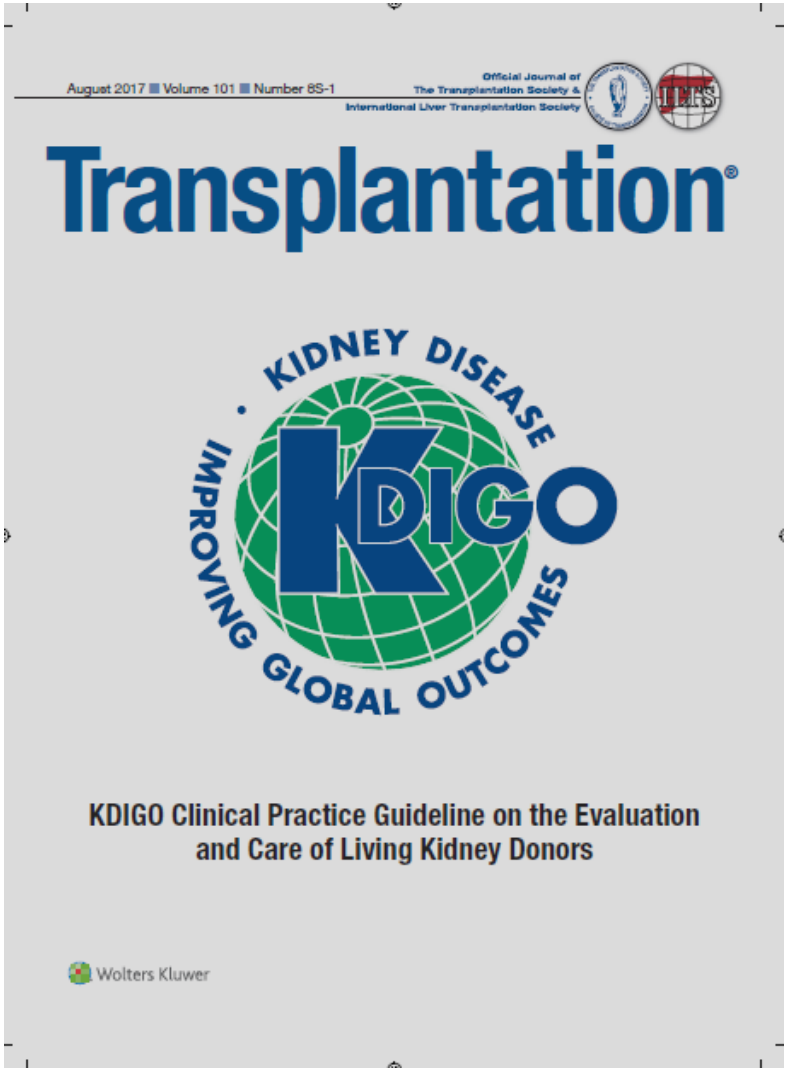


- Selecting **donors with minimal longterm risk** of **kidney failure** is important to **safeguard** the practice of kidney **donation**

- Equally important is **respecting the donor** candidates' autonomous **decisions** to seek the benefit and **accept the risk** of kidney donation

- **Balancing these objectives** requires careful **consideration of multiple measures** of health status of kidney donor candidates and the long-term consequences of kidney donation

Levey and Inker. GFR Evaluation in Living Kidney Donor Candidates. JASN.2017



Classification of GFR category		
Not acceptable for donation	Intermediate range	Acceptable for donation
< 60	60-89	≥90

(1) Donor candidacy is evaluated in light of long-term risk, in which **GFR is one of many factors. ESRD is considered a central outcome**

(2) **Two GFR thresholds** are used for decision- making: a **high** threshold **(>90 ml/min per 1.73m2)** to **accept** and a **low** threshold **(<60 ml/min per 1.73 m2)** to **decline**, with 60–89 ml/min per 1.73 m2 as an **intermediate range** in which the decision to accept or decline is made **on the basis of factors in addition to GFR.**

(3) **GFR is evaluated** using several methods available at the transplant center,including **estimating equations (eGFR) and clearance measurements (mGFR)**

- **Both** mGFR and eGFR are **associated with error** (bias and imprecision)

- The **accuracy of various methods for measuring and estimating** GFR are **not known with** sufficient **certainty** to define separate thresholds for each method

- The **mGFR** through nonisotopic external markers (inulin, ioexol, iothalamate) or isotopic techniques (125I iothalamate, EDTA-Cr51, 99Tc DTPA)- **gold standard** for the kidney failure evaluation

- Expensive , complexe, not available in many medical centers, not standardized, variation across centers

- **Despite the complexity**, GFR **should be more often measured as a confirmatory test** in clinical practice

- Should be limited to **special situations**.

-**Approximately 90% of centers used mClcr**

-other **10%** of centers used the clearance of an **exogenous filtration marker**

-approximately 67% of transplant centers used a threshold of >80 ml/min to accept donors

-25% used a threshold on the basis of age and sex

American Journal of Transplantation 2007; 7: 2333–2343
Blackwell Munksgaard

doi: 10.1111/j.1600-6143.2007.01932.x

The Medical Evaluation of Living Kidney Donors: A Survey of US Transplant Centers

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There are no conflicts of interest to report.

The use of living donors for kidney transplantation in the United States is common, and long-term studies have demonstrated the safety of donation by young, healthy individuals. However, transplant programs have little data to guide them in deciding which donors are unacceptable, and which characteristics are associated with kidney disease or poor psychosocial outcomes after donation. To document current practices in evaluating potential donors, we surveyed all US kidney transplant programs. Compared to a survey 12 years ago, medical criteria for donation are more inclusive in several areas. All responding programs now accept living unrelated donors. Most programs no longer have an upper age limit to be eligible. Programs are now more likely to accept donors with treated hypertension, or a history of kidney stones, provided that certain additional criteria are met. In contrast, medical criteria for donation are more restrictive in other areas, such as younger donor age and low creatinine clearance. Overall, significant variability remains among transplant programs in the criteria used to evaluate donors. These findings highlight the need for more data on long-term outcomes in various types of donors with potential morbidities related to donation.

passed deceased donors in 2001, and the use of living donors continues to rise (1). Minimal long-term risk has been demonstrated in studies comparing young, healthy individuals after nephrectomy with nondonating siblings (2), nonnephrectomized military recruits (3) or age-matched general populations (4,5). However, most of these studies are limited to the healthiest donors, and provide little information about different subsets of potential donors, such as those who are older, obese, hypertensive or have other characteristics potentially associated with renal disease. Decisions about which kidney donors to accept can affect the health outcomes of both donors and recipients.

In 1995, Bia et al. (6) published a survey of US transplant center practices in evaluating living renal donors. In part because of the continued lack of good data on donor outcomes, this survey about practices in 1992 was widely cited, and helped provide some guidelines about exclusion criteria. Since the publication of this survey, practices at US transplant centers likely have evolved. Reviews of how to evaluate kidney donors have been published (7,8), but actual practices have not been documented since Bia et al.'s 1995 study. To document current practices, and to help guide programs in developing protocols, we conducted an updated and expanded survey of US transplant programs.

Methods

We designed a 56-question web-based survey to gather information about living kidney donor evaluation and selection processes, including living donor types, alternative living donor programs, evaluation procedures, medical and psychosocial contraindications, informed consent policies and decision-making processes. We replicated the Bia et al.'s survey as much as possible, but expanded the questions in several areas. We omitted or modified some items that are addressed in other studies or are no longer

- Clinicians usually rely on endogenous **creatinine clearance** (mClcr)

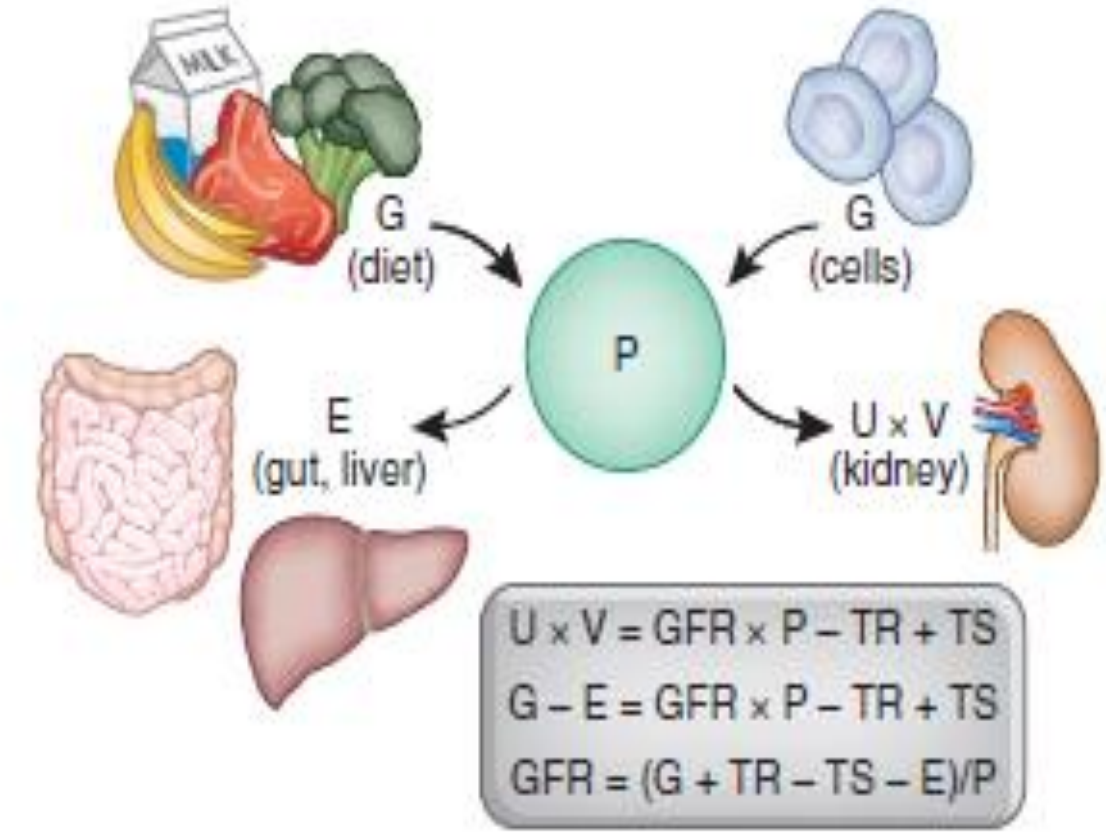
- Timed urine collections are **difficult to obtain** and **fraught with error**
  - underestimates if not correctly collected
  - overestimates due to tubular secretion (↑15% at normal GFR)

- **Creatinin** remains the **most frequent** marker **used** in clinical practice

- **Affected by age, gender and ethnicity** and these variables are taken into account in equations for prediction of GFR

- Equations **capture only the average relationship of surrogates** to some physiologic processes

Determinants of the serum level of endogenous filtration markers



Stevens and Levey. Measured GFR as a Confirmatory Test for Estimated GFR. JASN, 2009

- **Cystatin C** proposed as **superior marker** of GFR compared to creatininine (elderly diabetic patients free from kidney disease*)*

- **15/24** papers superior, **the rest- equal** performance

- **Not readily available**

- **Not standardized yet**

Leterza et al.Cystatin C: an improved estimator of glomerular filtration rate? Clin Chem 2002

- Cystatin C generation rate and serum levels have been **influenced by things independent of kidney function** (age, sex, cell turnover rate, steroid use, body mass index, inflammation, adiposity, thyroid diseases, certain malignancies, smoking....)

- **Extrarenal elimination** at **low levels of GFR**

Arici M. Management of Chronic Kidney Disease, Springer, 2014
Inker and Levey. National Kidney Foundation's Primer on Kidney Diseases , Elsevier Saunders, 2014

- **Using two filtration markers improves precision** of GFR estimates compared with using either marker alone

- **eGFRcr–cys is generally recommended** over eGFRcr or eGFRcys

Cockroft-Gault Equation

- The **oldest** but **simplest** equation
- **Derived** using data from **249 men with a Clcr 30–130 ml/min**

Cockcroft-Gault.Prediction of creatinine clearance from serum creatinine. Nephron, 1976

- Derived when **standardized creatinine assays were not in use**
- **With standardised** creatinine **assays**- **GFR overestimation (10–40 %)**
  - **Obese and elderly** patients (**overestimates**),
  - patients with **normal or mildly ↓ GFR** (**underestimates**)

- **Not adjusted for body surface area**
  - needs ideal body weight and not the actual one (DM patients are often obese- leads to overestimation)

Arici M. Management of Chronic Kidney Disease, Springer, 2014

MDRD Study Equation

- Developed in **1999-** data from **1628 CKD patients** (primarily white, nondiabetic) with **GFR 5 and 90 ml/min/1.73 m2**

Levey et al. A more accurate method to estimate glomerular filtration rate from serum creatinine: a new prediction equation. MDRD Study Group. Ann Intern Med, 1999

- The equation was **re-derived in 2006** for use with the **standardized serum creatinine** assays

Levey et al.Using standardized serum creatinine values in the modification of diet in renal disease study equation for estimating glomerular filtration rate. Ann Intern Med, 2006

- **Despite improvements in calibration**, MDRD **still underestimates GFRs > 90** ml/min/1.73 m2
- **Most widely used** formula, often **automatically reported**
- **Validation** needed for **different ethnic groups**

Arici M. Management of Chronic Kidney Disease, Springer, 2014

Soares AA et al. Glomerular filtration rate measurement and prediciton equations- review. Clin Chem Lab Med 2009

CKD-EPI Equation

- Derived in **2009-** large study **population (<u>with or without kidney disease</u>) with wide range of GFR**

Levey et al. A new equation to estimate glomerular filtration rate. Ann Intern Med, 2009

- When compared with MDRD, CKD-EPI **more accurate and with less bias, especially at ↑ GFR levels**.

Arici M. Management of Chronic Kidney Disease, Springer, 2014.

Which one is the best ?

Annals of Internal Medicine | Review

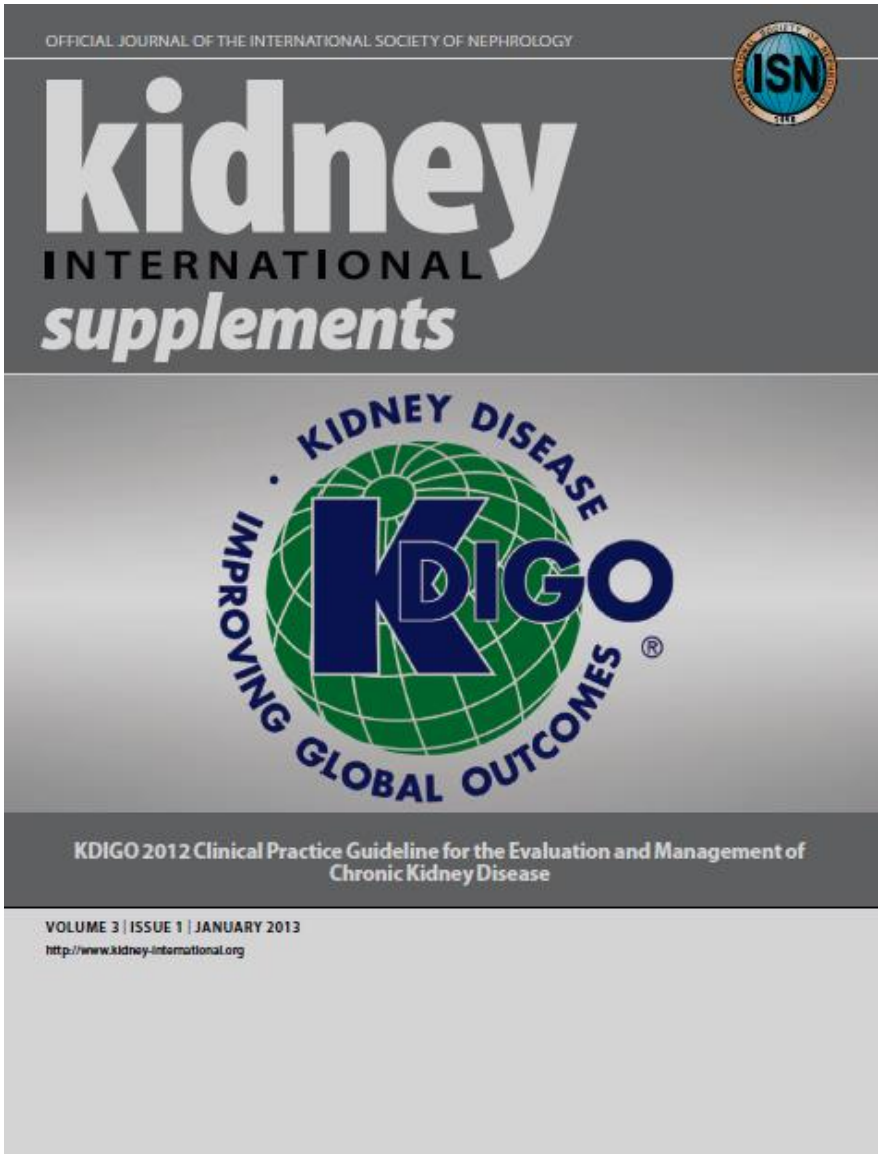
Estimating Equations for Glomerular Filtration Rate in the Era of Creatinine Standardization

A Systematic Review

Amy Earley, BS; Dana Miskulin, MD, MS; Edmund J. Lamb, PhD; Andrew S. Levey, MD; and Katrin Uhlig, MD, MS

- **Neither** GFR equation is **optimal for all** populations and GFR ranges.

- A **general practice** and public health perspective **favours** the **CKD-EPI** equation.



KIDNEY DISEASE IMPROVING GLOBAL OUTCOMES KDIGO

....use CKD-EPI equation for GFR estimation

- In **most circumstances, eGFR is sufficient** for clinical decision making.

- If GFR estimates are likely inaccurate or **if decisions** based on it **may have adverse consequences**, a **mGFR** is an important **confirmatory** test.

Stevens and Levey. Measured GFR as a Confirmatory Test for Estimated GFR. JASN, 2009

BRIEF REVIEW www.jasn.org

Measured GFR as a Confirmatory Test for Estimated GFR

Lesley A. Stevens and Andrew S. Levey

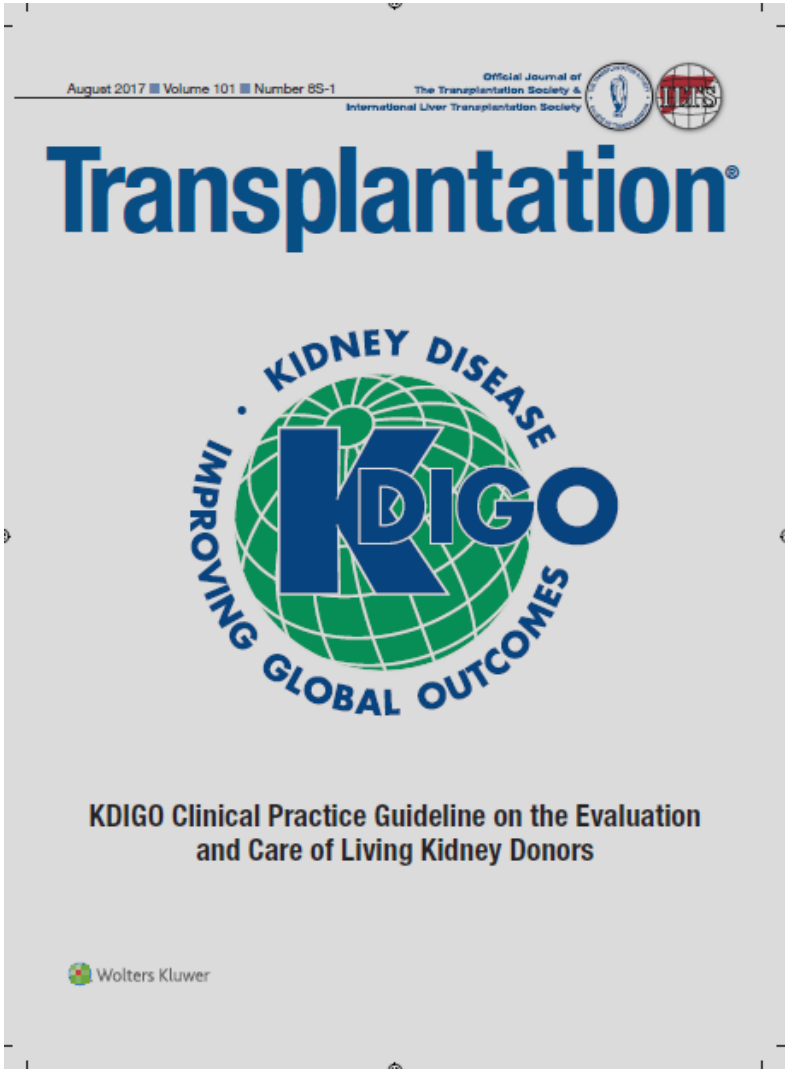
Tufts Medical Center, Boston, Massachusetts

Table 3. Indications for measured GFR

Extremes of age and body size
Severe malnutrition or obesity
Disease of skeletal muscle
Paraplegia or quadriplegia
Evaluation for kidney donation
Vegetarian diet
Before administration of prolonged courses of toxic medications

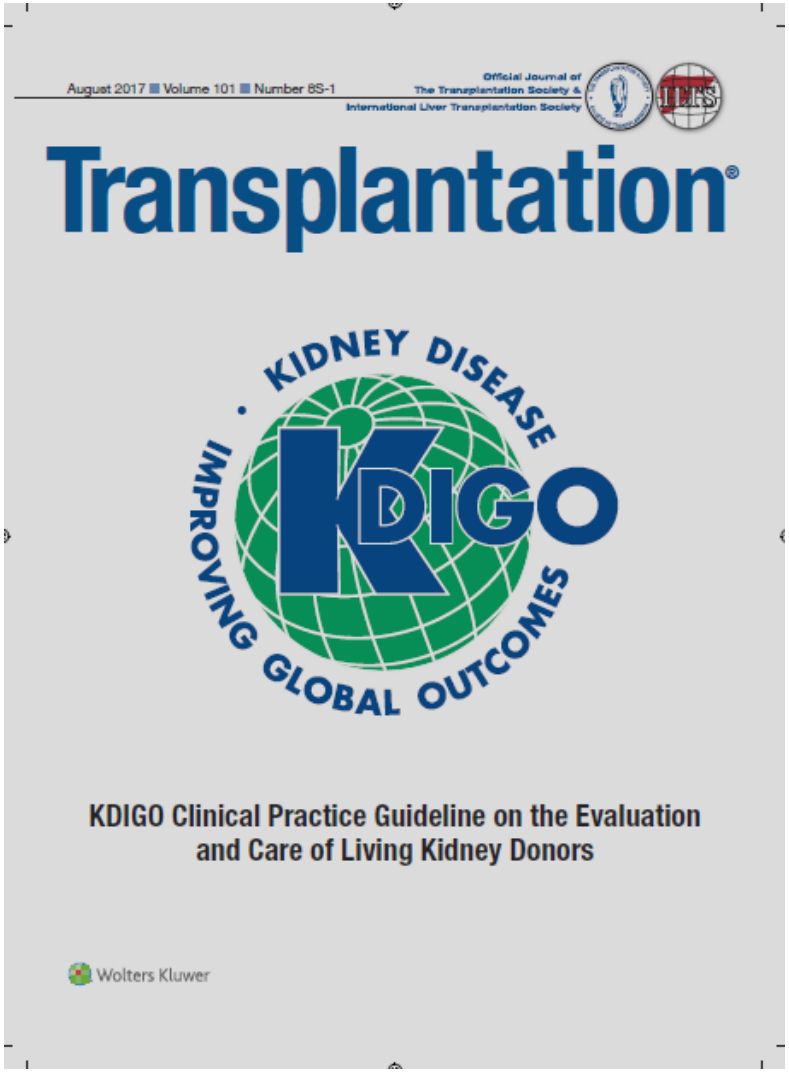
- **In individuals with normal renal function**, performance of the **eGFR** equations is frequently **sub-optimal with low overall accuracy** when results are compared with mGFR

- GFR estimation is **usually used as a screening test** but is **rarely sufficient to authorize donation** without further renal function evaluation



- **Two-stage testing** recommended in all donor candidates and **<u>using the best available method</u>** at the transplant center to assess GFR of donor candidates, recognizing that **more than one method may be available in many centers.**

- Donor GFR should be estimated from serum creatinine (**eGFRcr**) **for initial assessment**



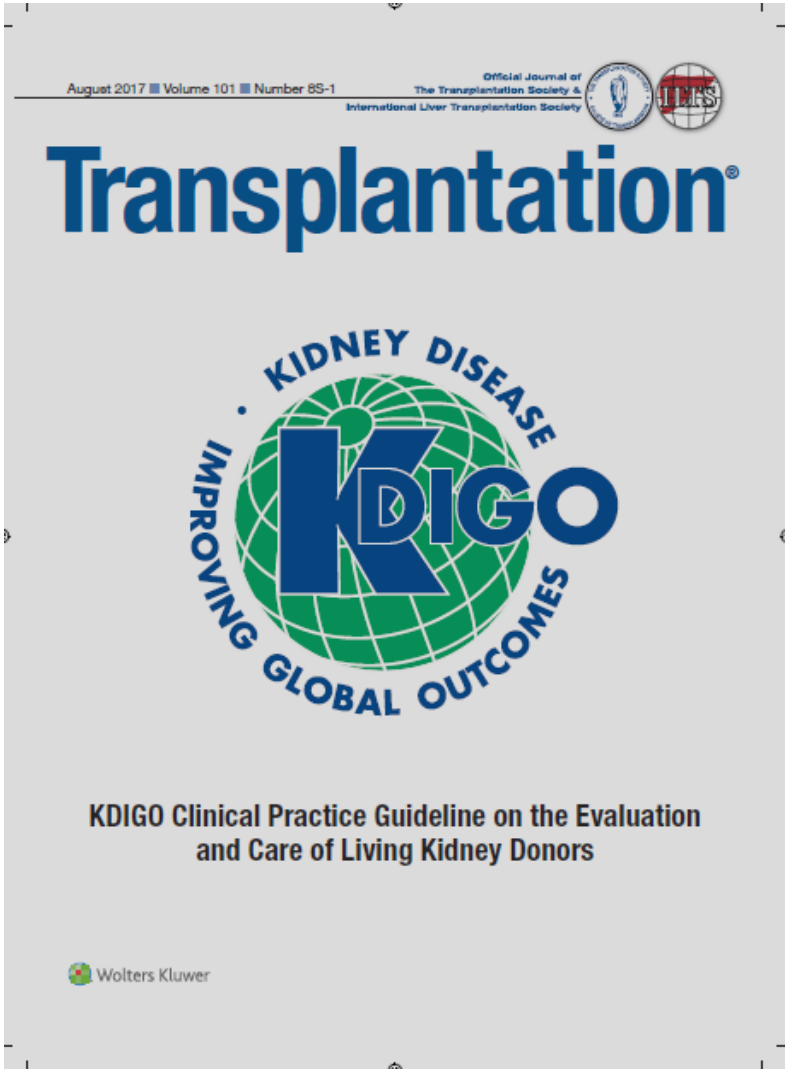
- Donor GFR **should be <u>confirmed</u>** using **<u>one or more</u>** of the following **measurements, depending on availability:**

- mGFR using an exogenous filtration marker, preferably U/P Cl of inulin, U/P Cl of iothalamate, U/P Cl of 51Cr-EDTA, U/P Cl of iohexol, or U Cl of 99mTc-DTPA

- mCrCl

- eGFRcr-cys

- repeat eGFRcr



If there are **parenchymal, vascular or urological <u>abnormalities</u> or <u>asymmetry</u> of kidney size** on renal imaging, **<u>single kidney GFR</u>** should be assessed using **radionuclides or contrast agents that are excreted by glomerular filtration** (eg, 99mTc-DTPA)

Evaluation of GFR is now receiving **increasing emphasis** because recent data demonstrate **increased risk of kidney disease after donation**, including a small increase in the risk of kidney failure

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Long-Term Consequences of Kidney Donation

Hassan N. Ibrahim, M.D., Robert Foley, M.B., B.S., LiPing Tan, M.D., Tyson Rogers, M.S., Robert F. Bailey, L.P.N., Hongfei Guo, Ph.D., Cynthia R. Gross, Ph.D., and Arthur J. Matas, M.D.

CONCLUSIONS

Survival and the risk of ESRD in carefully screened kidney donors appear to be similar to those in the general population. Most donors who were studied had a preserved GFR, normal albumin excretion, and an excellent quality of life.

Long-term risks for kidney donors

Geir Mjøen[1], Stein Hallan[2,3], Anders Hartmann[1], Aksel Foss[1], Karsten Midtvedt[1], Ole Øyen[1], Anna Reisæter[1], Per Pfeffer[1], Trond Jenssen[1], Torbjørn Leivestad[4], Pål- Dag Line[1], Magnus Øvrehus[2], Dag Olav Dale[1], Hege Pihlstrøm[1], Ingar Holme[5], Friedo W. Dekker[6] and Hallvard Holdaas[1]

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Previous studies have suggested that living kidney donors maintain long-term renal function and experience no increase in cardiovascular or all-cause mortality. However, most analyses have included control groups less healthy than the living donor population and have had relatively short follow-up periods. Here we compared long-term renal function and cardiovascular and all-cause mortality in living kidney donors compared with a control group of individuals who would have been eligible for donation. All-cause

Living donor kidney transplantation is the preferred treatment for end-stage renal disease (ESRD), because it is associated with improved graft and patient survival compared with transplantation from a deceased donor.[1] Living kidney donation, however, requires that healthy individuals voluntarily undergo major surgery with no physical health benefit to themselves. Although rare, perioperative mortality does occur during organ retrieval from living donors and have been estimated to occur in 0.2% of liver donors and

donors. Thus, kidney donors are at increased long-term risk for ESRD, cardiovascular, and all-cause mortality compared with a control group of non-donors who would have been eligible for donation.

incidence of ESRD among donors was 302 cases per million and might have been influenced by hereditary factors. Immunological renal disease was the cause of ESRD in the donors. Thus, kidney donors are at increased long-term risk for ESRD, cardiovascular, and all-cause mortality compared with a control group of non-donors who would have been eligible for donation.

control groups. In most studies, controls were selected from the general population, which includes adults with medical conditions that would make them indigible for kidney donation.[10–12] As a result, these controls would have been less healthy than the living donors and an effect of organ donation on all-cause and cardiovascular mortality could have been underestimated. Three studies have induded

Original Investigation

Risk of End-Stage Renal Disease Following Live Kidney Donation

Abimereki D. Muzaale, MD, MPH; Allan B. Massie, PhD; Mei-Cheng Wang, PhD; Robert A. Montgomery, MD, DPhil; Maureen A. McBride, PhD; Jennifer L. Wainright, PhD; Dorry L. Segev, MD, PhD

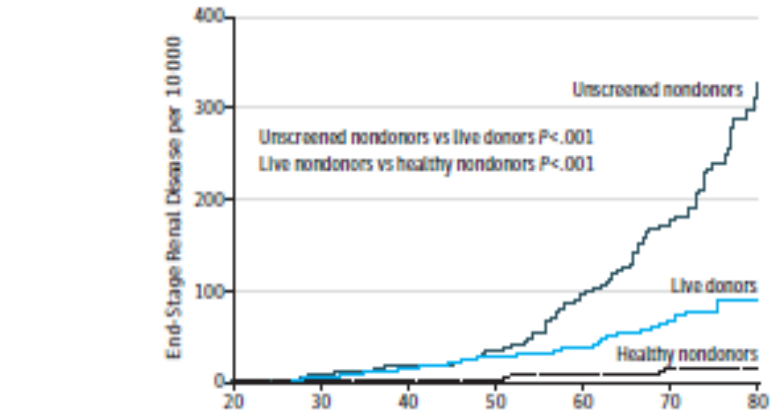
CONCLUSIONS AND RELEVANCE Compared with matched healthy nondonors, kidney donors had an increased risk of ESRD over a median of 7.6 years; however, the magnitude of the absolute risk increase was small. These findings may help inform discussions with persons considering live kidney donation.

Editorial page 577

Supplemental content at jama.com

JAMA. 2014;311(6):579-586. doi:10.1001/jama.2013.285141

Figure 3. Estimated Lifetime Risk of End-Stage Renal Disease in Matched But Unscreened Nondonors, Live Kidney Donors, and Matched Healthy Nondonors



No. at risk							
Unscreened nondonor	1296	18436	36272	40863	26982	7990	647
Live donor	1143	13144	22647	22944	12151	2575	218
Healthy nondonor	1306	18487	36397	40961	28358	9011	870

Nephrol Dial Transplant (2017) 32: 216–223
doi: 10.1093/ndt/gfw429

ndt
Nephrology Dialysis Transplantation

NDT Perspectives

Long-term risks of kidney living donation: review and position paper by the ERA-EDTA DESCARTES working group

Umberto Maggiore[1], Klemens Budde[2], Uwe Heemann[3], Luuk Hilbrands[4], Rainer Oberbauer[5], Gabriel C. Oniscu[6], Julio Pascual[7], Soren Schwartz Sorensen[8], Ondrej Viklicky[9] and Daniel Abramowicz[10] for the ERA-EDTA DESCARTES working group

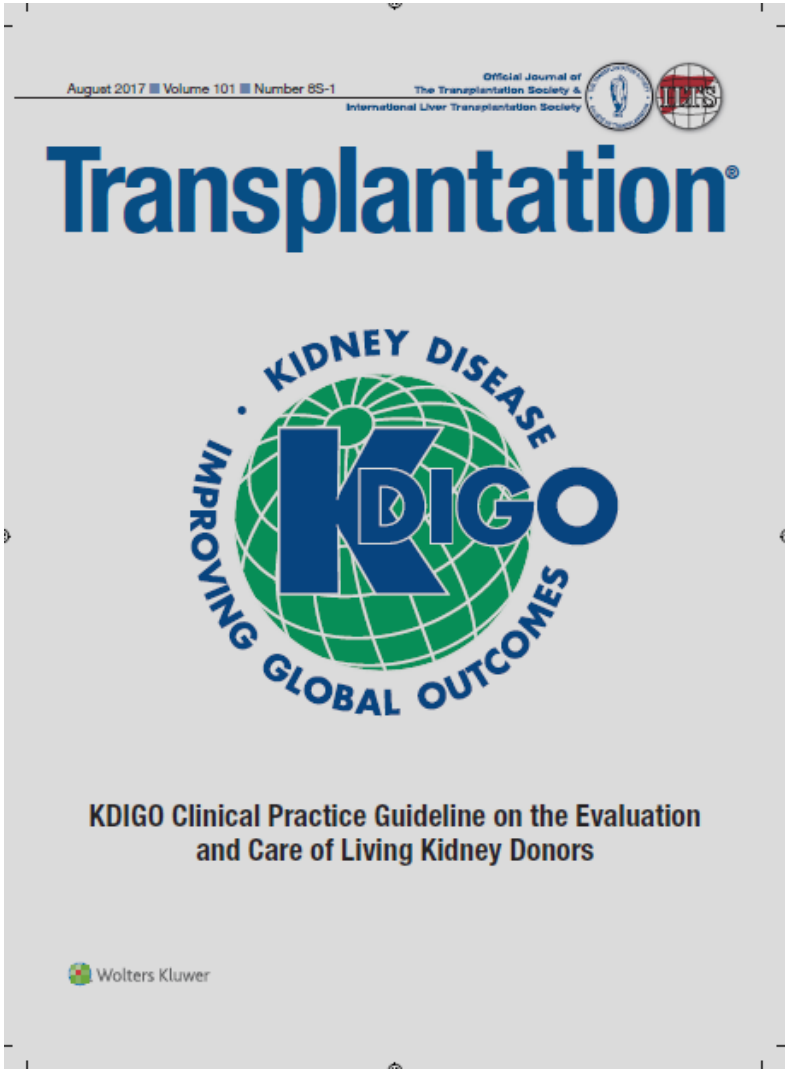
[1]Department of Nephrology, Azienda Ospedaliero-Universitaria di Parma, Parma, Italy, [2]Department of Nephrology, Charité Medical University Berlin, Berlin, Germany, [3]Department of Nephrology, Technical University of Munich, Munich, Germany, [4]Department of Nephrology, Radboud University Medical Centre, Nijmegen, The Netherlands, [5]Department of Nephrology, Medical University of Vienna, Vienna, Austria,

- Average absolute risk was in fact <0.3% after 15 years in the US studies (i.e. **>300 living donations need to occur to have one donor** develop nephrectomy-related **ESRD**)

- Norwegian study showed that **subjects with a first-degree relative with ESRD** caused by **non-hereditary diseases** (glomerulonephritis, pyelonephritis, diabetes or hypertension) have a **long-term risk of ESRD almost 4 times higher** compared with subjects with no family history of renal disease.

- **Consanguinity in young donors** can be regarded **per se** as a **risk factor** for the development of renal diseases **despite a normal medical workup**

- **African American** race is an additional **baseline risk indicator** that might be taken into account when assessing young related donors with a normal workup



Counseling

- We suggest that **donor candidates be informed** that the future **risk of developing kidney failure** necessitating treatment with dialysis or transplantation **is slightly higher because of donation**; however, **average absolute risk in the 15 years following donation remains low**

- Whether or not GFR **should be measured** rather than **estimated in this population?**

Evaluation of Creatinine-Based Estimates of Glomerular Filtration Rate in a Large Cohort of Living Kidney Donors

Naim Issa,[1] Kathryn H. Meyer,[2] Susana Arrigain,[2] Gautam Choure,[3] Richard A. Fatica,[1] Saul Nurko,[1] Brian R. Stephany,[1] and Emilio D. Poggio[1,4]

Background. Accurate determination of kidney function is critical in the evaluation of living kidney donors and higher donor glomerular filtration rate (GFR) is associated with better allograft outcomes. However, among transplant centers donor kidney function evaluation varies widely.

Methods. The performance of creatinine clearance (CrCl), Modification of Diet in Renal Disease (MDRD), the re-

^{125}I-iothalamate GFR (iGFR)

dardized

yzed in 4

423 donors.

roft-Gault (CG) formula as compared with GFR measurement were then evaluated for their association with graft function at 1 year.

Results. The MDRD and re-expressed MDRD equations underestimated iGFR whereas CG showed minimal bias (median difference=−11.0, −16.3, and −0.5 mL/min/1.73 m^2, respectively). CrCl overestimated iGFR (10 mL/min/1.73 m^2). The MDRD, re-expressed MDRD, and CG formulas were more accurate (88%, 86%, and 88% of estimates within 30% of iGFR, respectively) than CrCl (80% within 30% of iGFR). Interestingly, low bias and high accuracy were achieved by averaging the MDRD estimation with the CrCl result; both methods available to the clinician in most transplant centers. We also showed that predonation GFR as measured by isotopic renal clearance or any of the creatinine-based estimation formulas may be associated with allograft function at 1 year, whereas the widely used CrCl was not.

Conclusions. Variable performance was seen among different GFR estimations, with CrCl being the poorest.

recommendations to use the MDRD equation with standardized serum creatinine did not improve its performance.

However, recognizing the limited availability of GFR laboratories, still clinically useful if used with caution and understanding their limitations.

Keywords: Glomerular filtration rate, MDRD, Creatinine clearance, Living donor, Kidney transplantation.

(*Transplantation* 2008;86: 223–230)

ELSEVIER CrossMark

Transplantation Proceedings, 47, 2603–2607 (2015)

Assessment of the Renal Function in Potential Donors of Living Kidney Transplants: Expanded Study

L.B. Macías[a,*], M.S. Poblet[a], N.N. Pérez[a], R.I. Jerez[b], F.M. Gonzalez Roncero[a], G.B. Blanco[a], M.A.P. Valdivia[a], A.S. Benjumea[a], and M.A. Gentil Govantes[a]

[a]UGC-Nefrourológica and [b]y Medicina Nuclear, Hospital Virgen del Rocío, Sevilla, SpainF.M. Gonzalez Roncero

ABSTRACT

Introduction. It is very important to determine as accurately as possible the renal function in potential living renal transplant donors, especially those with limited renal function (CrCl <90 mL/m/1.73 m^2), age older than 50 years, and cardiovascular risk factors that might favor the development of long-term kidney diseases.

Objective. The objective of this study was to compare the direct measurement of glomerular filtration rate (GFR) using EDTA-Cr51 e estimations based on creatinine (eGFR): Cr clearance (CCr) with 24-hour urine and estimated using Cockroft-Gault (adjusted by using body surface area–Mosteller formula-SC), MDRD-4, MDRD-6, and CKD-EPI to determine the usefulness of different methods from EDTA-Cr51to evaluate the kidney function.

Patients and Methods. The kidney function evaluation has been made to 105 donors kidney donors using the EDTA-Cr51 method. The GFR obtained through the EDTA-Cr51 is compared with the CCr values in 24-hour urine and eGFR based on creatinine (Cockcroft-Gault, MDRD4, MDRD6, and CKD-EPI).

Results. Using the Bland Altman graphic we have observed that the most dispersed results are obtained with the eGFR using CCr in 24-hour urine and CKD-EPI. By means of Pasing & Bablock, we realized that MDRD-4 and MDRD-6 show the highest approximation to the reference method proposed to be substituted, whereas CCr shows a high dispersion.

Conclusions. MDRD-4 and MDRD-6 formulas reveal the best adjustment to the measure by EDTA-Cr51. This might represe the best option if a direct eGFR measure not available.

CKD-EPI Instead of MDRD for Candidates to Kidney Donation

Pablo R. Lujan,[1,3] Carlos Chiurchiu,[2] Walter Douthat,[2] Javier de Arteaga,[2] Jorge de la Fuente,[2] Raul H. Capra,[1] and Pablo U. Massari[2]

Background. The determination of the glomerular filtration rate (GFR) is critical for the selection of a potential kidney donor. The complex and impractical techniques for the measurement of GFR have led to the development of equations to estimate GFR. Modification of diet in renal disease (MDRD) formula is the most widely used but its performance is poor because it systematically underestimates GFR above 60 mL/min. A new formula called the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) seems to overcome this limitation but needs to be tested in healthy potential kidney donors.

Methods. From 2007 to 2011, a cross-sectional study was performed on 85 adults who were candidates for living-related kidney donation. GFR was measured by nonradiolabeled iothalamate clearance determined by high-performance liquid chromatography, and renal function was estimated by using CKD-EPI and MDRD equations. The overall performance of the equations was analyzed, and the estimation for GFR above 90 mL/min was studied by means of receiver operating characteristic curves.

Results. The mean (SD) (range) of the measured GFR was 116 (24) (64–160) mL/min per 1.73 m^2, estimated GFR with CKD-EPI was 108 (22) (64–153) mL/min per 1.73 m^2, and MDRD was 99 (28) (46–157) mL/min per 1.73 m^2. CKD-EPI presented lower bias (3.3 vs. 10.2 mL/min/1.73 m^2), higher precision [interquartile range (minimum value-maximum value), 25 (53–140) vs. 32 (43–161) ml/min] and higher accuracy (100% vs. 89%) compared with MDRD.

Conclusion. The CKD-EPI equation had a higher performance than the MDRD equation in the GFR estimation of healthy population. CKD-EPI is applicable instead of MDRD, to subjects or candidates for kidney donation to avoid wrong GFR underestimates, which may lead to an inappropriate exclusion of candidates.

Keywords: Iothalamic acid, Glomerular filtration rate, Chronic kidney disease.

(*Transplantation* 2012;94: 637–641)

OPEN ACCESS Freely available online

PLOS | ONE

Comparison of Estimating Equations for the Prediction of Glomerular Filtration Rate in Kidney Donors before and after Kidney Donation

Byung Ha Chung[1,2], Jee Hyun Yu[1,2], Hyuk Jin Cho[3], Ji-Il Kim[4], In Sung Moon[4], Cheol Whee Park[1,2], Chul Woo Yang[1,2], Yong-Soo Kim[1,2], Bum Soon Choi[1,2]*

1 Transplant research center, Seoul St. Mary's Hospital, College of Medicine, The Catholic University of Korea, Seoul, Korea, **2** Division of Nephrology, Department of Internal Medicine, Seoul St. Mary's Hospital, College of Medicine, The Catholic University of Korea, Seoul, Korea, **3** Department of Urology, Seoul St. Mary's Hospital, College of Medicine, The Catholic University of Korea, Seoul, Korea, **4** Department of Surgery, Seoul St. Mary's Hospital, College of Medicine, The Catholic University of Korea, Seoul, Korea

Abstract

The aim of this study is to investigate the usefulness of the GFR-estimating equations to predict renal function in kidney donors before and after transplantation. We compared the performance of 24-hour-urine–based creatinine clearance (24 hr urine-CrCl), the Cockcroft-Gault formula ($eGFR_{CG}$), the Modification of Diet in Renal Disease equation ($eGFR_{MDRD}$), and the Chronic Kidney Disease Epidemiology Col[illegible] diethylenetriaminepentaacetic (^{99m}Tc-DTPA) [illegible]learance (mGFR) in 207 [illegible]. Before donation, $eGFR_{CKD-EPI}$ showed minimal bias and did not show a significant difference from mGFR ($P = 0.09$, respectively) while 24 hr urine-CrCl and $eGFR_{MDRD}$ significantly underestimated mGFR ($P<0.001$ for each). Precision and accuracy was highest in $eGFR_{CKD-EPI}$ and this better performance was more dominant when renal function is higher than 90 $mL \cdot min^{-1} \cdot 1.73\ m^{-2}$. After kidney donation, $eGFR_{MDRD}$ was superior to other equations in precision and accuracy in contrast to before donation. Within individual analysis, $eGFR_{MDRD}$ showed better performance at post-donation compared to pre-donation, but $eGFR_{CKD-EPI}$ and $eGFR_{CG}$ showed inferior performance at post-donation. In conclusion, $eGFR_{CKD-EPI}$ [illegible]ved better performance compared to other equations before donation. In a uninephric donor, however, [illegible]re appropriate for the estimation of renal function than $eGFR_{CKD-EPI}$.

207 potential kidney donors

Renal Function Equations before and after Living Kidney Donation: A Within-Individual Comparison of Performance at Different Levels of Renal Function

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Background and objectives: The Modification of Diet in Renal Disease (MDRD) study equation and the Cockcroft-Gault (CG) equation perform poorly in the (near-) normal range of GFR. Whether this is due to the level of GFR as such or to differences in individual characteristics between healthy individuals and patient with chronic kidney disease (CKD) is unknown.

Design, setting, participants, & measurements: We evaluated the performance of MDRD, CG per BSA ($CG/_{BSA}$) and Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equations compared with measured GFR (I-iothalamate) at 4 months before and 2 months after donation in 253 consecutive living kidney donors.

Results: mGFR declined from 103 ± 15 to 66 ± 11 ml/min per 1.73 m^2 after donation. All equations underestimated mGFR at both time points. Arithmetic performance analysis showed improved performance after donation of all equations, with significant reduction of bias after donation. Expressed as percentage difference, mGFR–estimated GFR (eGFR) bias was reduced after donation only for $CG/_{BSA}$. Finally, in 295 unselected individuals who were screened for donation, mGFR was below the cutoff for donation of 80 ml/min per 1.73 m^2 in 19 individual but in 166, 98, and 74 for MDRD, CDK-EPI, and $CG/_{BSA}$, respectively.

Conclusions: A higher level of GFR as such is associated with larger absolute underestimation of true GFR. For donor screening eGFR should be interpreted with great caution; in doubt, true GFR should be performed to prevent unjustif

Clin J Am Soc Nephrol 5: 1960–1968, 2010. doi: 10.2215/CJN.08761209

Int Urol Nephrol (2015)
DOI 10.1007/s11255-014-0859-y

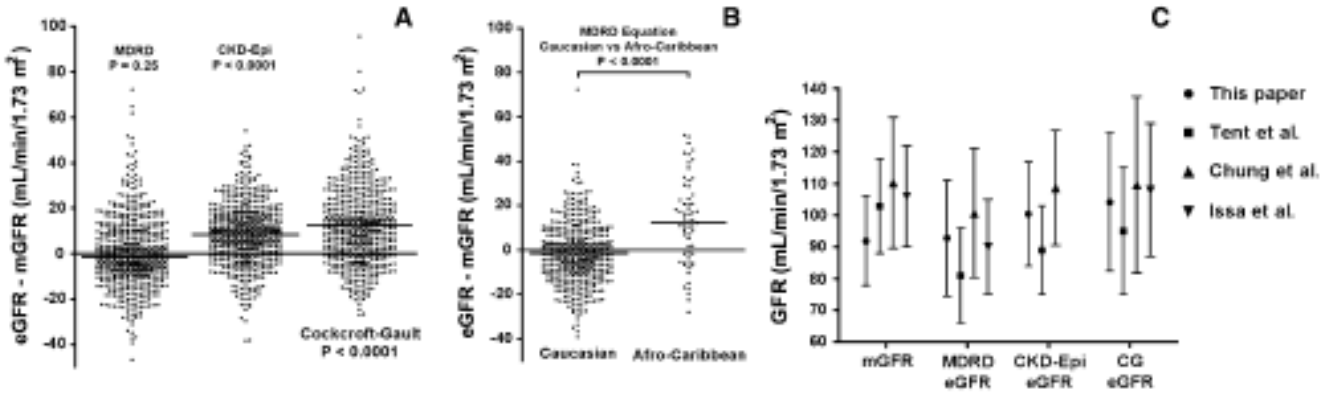
NEPHROLOGY - ORIGINAL PAPER

Comparison of estimated GFR and measured GFR in prospective living kidney donors

Thakshyanee Bhuvanakrishna · Glen M. Blake · Rachel Hilton · Lisa Burnapp · Christopher Sibley-Allen · David Goldsmith

^{51}Cr-EDTA
508 donors.

Conclusions The level of agreement between mGFR and all three eGFR values was poor, with the MDRD equation performing best. We conclude that reliance on creatinine-based eGFR values is unsatisfactory for the evaluation of potential living kidney donors.



Modification of Diet in Renal Disease Equation Underestimates Glomerular Filtration Rate in Egyptian Kidney Donors

Salwa Ibrahim,[1] Laila Rashid[2]

Abstract

Objectives: **Inulin clearance and radioisotope studies are the most accurate means of measuring glomerular filtration rates (GFRs). The Kidney Disease Outcomes Quality Initiative guidelines recommend estimating GFRs with the Modification of Diet in Renal Disease (MDRD) or the Cockcroft-Gault equation. We examined the accuracy of the MDRD equation and creatinine clearance based on 24-hour urine collection to predict GFRs in a group of healthy donors.**

Materials and Methods: **We examined the medical records of 100 kidney donors who had undergone ^{99m}Tc-diethylenetriamine-pentaacetic acid (DTPA) renal clearance and creatinine clearance measurements at the transplant outpatient clinic of Cairo University Hospital in Cairo, Egypt, between June 2002 and July 2006. GFR was predicted with the abbreviated MDRD formula. We examined significant differences, potential correlations, and agreements between GFR as predicted and as positive correlation was observed when creatinine clearance and ^{99m}Tc-DTPA-measured GFR were compared (R=0.451; *P* = .000). No significant correlation was noted between $eGFR_{MDRD}$ and ^{99m}Tc-DTPA-measured GFRs (R=0.126; *P* = .211). A Bland-Altman analysis showed poor agreement between GFR_{MDRD} and creatinine clearance on the one hand and measured GFR on the other.**

Conclusions: **Neither the MDRD equation nor creatinine clearance is accurate in predicting GFRs in healthy donors.**

Experimental and Clinical Transplantation (2008)

Introduction

An accurate estimation of the glomerular filtration rate (GFR) is essential in assessing prospective kidney donors. Inulin clearance and radioisotope studies are the most accurate means of measuring GFR, but they are cumbersome and expensive (1). The new Kidney

Clin Exp Nephrol (2010) 14:63–67
DOI 10.1007/s10157-009-0224-0

ORIGINAL ARTICLE

Utility of the Japanese GFR estimation equation for evaluating potential donor kidney function

Yoichi Kakuta · Masayoshi Okumi · Naotsugu Ichimaru · Toyofumi Abe · Norio Nonomura · Akihiko Okuyama · Yasuyuki Kojima · Yoshitaka Isaka · Shiro Takahara · Enyu Imai · Masaru Horio

Received: 13 May 2009 / Accepted: 17 August 2009 / Published online: 6 October 2009

Abstract

Background In Japan, the number of living kidney transplantations has increased each year, and an accurate evaluation of renal function must be conducted before donation to minimize the risk to donors. Recently, the Japanese Society of Nephrology issued a new equation for estimating glomerular filtration rate (eGFR) in Japanese people. This study compared the accuracy of eGFR and creatinine clearance (Ccr) values with that of inulin clearance (Cin) for assessing renal function in kidney donors.

Methods Clinical data were analyzed for 85 potential living kidney donors who had undergone routine measured GFR (mGFR) and Ccr measurements from October 2006 to November 2008 at a single center. Inulin clearance, representing the mGFR, was determined by standard method. The eGFR was calculated as: $eGFR = 194 \times Scr^{-1.094} \times Age^{-0.287}$ (for females, $\times 0.739$).

Results Mean mGFR was 96.1 ± 14.7 (range 67.8–126.8); mean eGFR, 72.6 ± 12.7 (range 50.1–107.1); and mean Ccr, 117.3 ± 22.4 (range 35.1–170.1), in units of ml/min/1.73 m^2 for each. Relative to mGFR, the correlation coefficient for Ccr was 0.496, and the mean difference between the two values was 21.1 ml/min/1.73 m^2 (23.2%), with a root-mean square error (RMSE) of 19.6. The correlation coefficient between eGFR and mGFR was 0.502, and the mean difference between the two values was −23.5 (23.7%), with a RMSE of 11.0. Bland–Altman plots showed that Ccr overestimated mGFR in 90.6% of cases, whereas eGFR underestimated mGFR in 95.3% of cases.

Conclusion Ccr and eGFR values did not accurately estimate mGFR in Japanese living kidney donors.

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Clin Transplant 2009: 23: 469–475 DOI: 10.1111/j.1399-0012.2009.01027.x

Clinical Transplantation

A comparison of prediction equations for estimating glomerular filtration rate in Chinese potential living kidney donors

Zhao W-Y, Zeng L, Zhu Y-H, Wang L-M, Zhou M-S, Han S, Zhang L. A comparison of prediction equations for estimating glomerular filtration rate in Chinese potential living kidney donors.
Clin Transplant 2009: 23: 469–475. © 2009 John Wiley & Sons A/S.

Abstract: Background: Accurate measurement of donor renal function has important long-term implications for both donors and recipients. In clinical practice, renal function may be estimated by using 24-h urinary creatinine clearance (urine-CrCl) and various specifically derived prediction equations. We assessed the suitability of urine-CrCl and prediction equations for evaluating Chinese kidney donors.
Methods: A total of 224 donors who had undergone ^{99m}Tc-diethylenetriaminepentaacetic acid glomerular filtration rate (GFR) estimation were enrolled. We evaluated the performance of the Cockcroft–Gault equation (CG-CrCl), the CG-CrCl equation corrected for GFR (CG-GFR), the isotope dilution mass spectrometry traceable modification of diet in renal disease (IDMS-MDRD) study equation, the new MDRD study equation for Chinese (C-MDRD 1), the modified MDRD study equation with a Chinese coefficient (C-MDRD 2), the modified IDMS-MDRD study equation with a Japanese coefficient (J-MDRD), and urine-CrCl in predicting GFR before donation.
Results: Of 224 donors selected, 68 were male and 156 were female. Of all the prediction equations, C-MDRD 1 was the least scattered and most precise. However, predictive performance was poor for all the equations.
Conclusion: The performance of urine-CrCl and all the equations was disappointing, and even the best performing equation C-MDRD 1 was unacceptable. Considering the potential risk of living kidney donation, other more accurate methods of GFR measurement should be used in clinical practice.

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Key words: ^{99m}Tc-diethylenetriaminepentaacetic acid – creatinine clearance – donor evaluation – glomerular filtration rate – prediction equations

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Accepted for publication 4 May 2009

- **If measures are not consistent**, an evaluation of the likely sources of error can suggest which measure is more likely to be correct:
  - a lower eGFRcr and eGFRcr–cys but higher eGFRcys, mClcr, and mGFR suggests increased creatinine generation rather than low true GFR
  - a higher eGFRcr, eGFRcr–cys, and mGFR but lower mClcr suggests an incomplete 24-hour urine collection
  - a higher eGFRcr, eGFRcr–cys, and mClcr but lower mGFR suggests a GFR measurement error.

- Despite the well recognized imprecision of **eGFR at higher levels**, it is **helpful to interpret** clearance **measurements** and **detect** a possible **error**.

- It can **provide substantial information** to estimate the **probability** that **mGFR is above or below** the thresholds for decision-making.

- There is a need for a strategy to **identify** potential donors **who should undergo** GFR **measurement.**

- **Web-based application** to compute the **probability**, based on eGFR, that **mGFR** for a donor candidate **is above or below** a range of **thresholds** useful in living donor evaluation and selection

- The probabilities used to develop the tool were **calculated from large cohorts,** including NHANES and CKD-EPI

- The authors suggest that this application **could be used** to **identify** donors **requiring** GFR **measurement**

- ...but were not applied to a cohort of potential living kidney donors

Huang et al. Estimated GFR for Living Kidney Donor Evaluation. AmJTransplant 2016

Donor Candidate GFR Calculator: Determining Probability of GFR Above or Below Certain Threshold

The data below are derived from Huang N, Foster M, Lentine K et al. Estimated GFR for living kidney donor evaluation. *American Journal of Transplantation* [epub ahead of print Nov 23 2015].

Step 1: Describe your patient

Age	50	years
Sex	○ Male ◉ Female	
Race	◉ Non Black ○ Black	
Creatinine	1	◉ mg/dL ○ µmol/L
Cystatin C	1.1	mg/L
eGFRcr		
eGFRcr-cys		

Step 2: Determine pre-test probability

Calculate pre-test probability

Result (Pre-test probability based on age, sex and race from US population data)

Measured GFR Thresholds			
<60	<70	≥80	≥90
6	12	77	64

Percentage of NHANES participants who had eGFRcr-cys less or above the specified thresholds. If you are interested in the opposite of the threshold (eg < 80), then subtract the value given from 100.

You can use the numbers above or a different number based on knowledge of your patient's medical history. For example, if your patient has a strong family history of CKD, you may wish to alter the pretest probability. If so, write the number to be used as pre-test probability in table below.

Measured GFR Thresholds			
<60	<70	≥80	≥90
6	12	77	64

Step 3: Calculate the post-test probability

The calculator will look up the likelihood ratio based on the eGFR calculated from the creatinine and cysatin provided above and will compute post-test probability.

Calculate post-test probability

	Measured GFR Thresholds			
	<60	<70	≥80	≥90
Post-test probability from eGFRcr†	4	15	52	18
Post-test probability from eGFRcr-cys‡	2	19	20	2

†**Post test probability of mGFR above or below the threshold based on eGFRcr.** If you are interested in the opposite of the threshold (eg < 80), then subtract the value given from 100.

‡**If you also indicated the eGFRcr-cys, the calculator will use the post-test probability from the eGFRcr as the pre-test probability and use it to compute the post-test probability from eGFRcr-cys.** If you are interested in the opposite of the threshold (eg < 80), then subtract the value given from 100.

Summary report

Based on the information supplied:

Age	50
Sex	Female
Race	Non Black
Creatinine	1 mg/dL
Cystatin C	1.1 mg/L
Estimated GFR from creatinine	66 ml/min per 1.73 m²
Estimated GFR from creatinine-cystatin C	66 ml/min per 1.73 m²

	Measured GFR Thresholds			
	<60	<70	≥80	≥90
Pre-test probability	6	12	77	64
Post-test probability from eGFRcr†	4	15	52	18
Post-test probability from eGFRcr-cys‡	2	19	20	2

†**Post test probability of mGFR above or below the threshold based on eGFRcr.** If you are interested in the opposite of the threshold (eg < 80), then subtract the value given from 100.

‡**If you also indicated the eGFRcr-cys, the calculator will use the post-test probability from the eGFRcr as the pre-test probability and use it to compute the post-test probability from eGFRcr-cys.** If you are interested in the opposite of the threshold (eg < 80), then subtract the value given from 100.

Print summary

American Journal of Transplantation 2016; 16: 3024–3032
Wiley Periodicals Inc.

doi: 10.1111/ajt.13908

Brief Communication

Estimated or Measured GFR in Living Kidney Donors Work-up?

F. Gaillard[1,*], M. Flamant[2,†], S. Lemoine[3,†], S. Baron[4,†], M.-O. Timsit[5], D. Eladari[6], C. Fournier[1], C. Prot-Bertoye[4], J.-P. Bertocchio[4], E. Vidal-Petiot[2], L. Lamhaut[7], E. Morelon[8], M.-N. Péraldi[9], F. Vrtovsnik[10], G. Friedlander[11], A. Méjean[5], P. Houillier[12], C. Legendre[1,†] and M. Courbebaisse[11,†]

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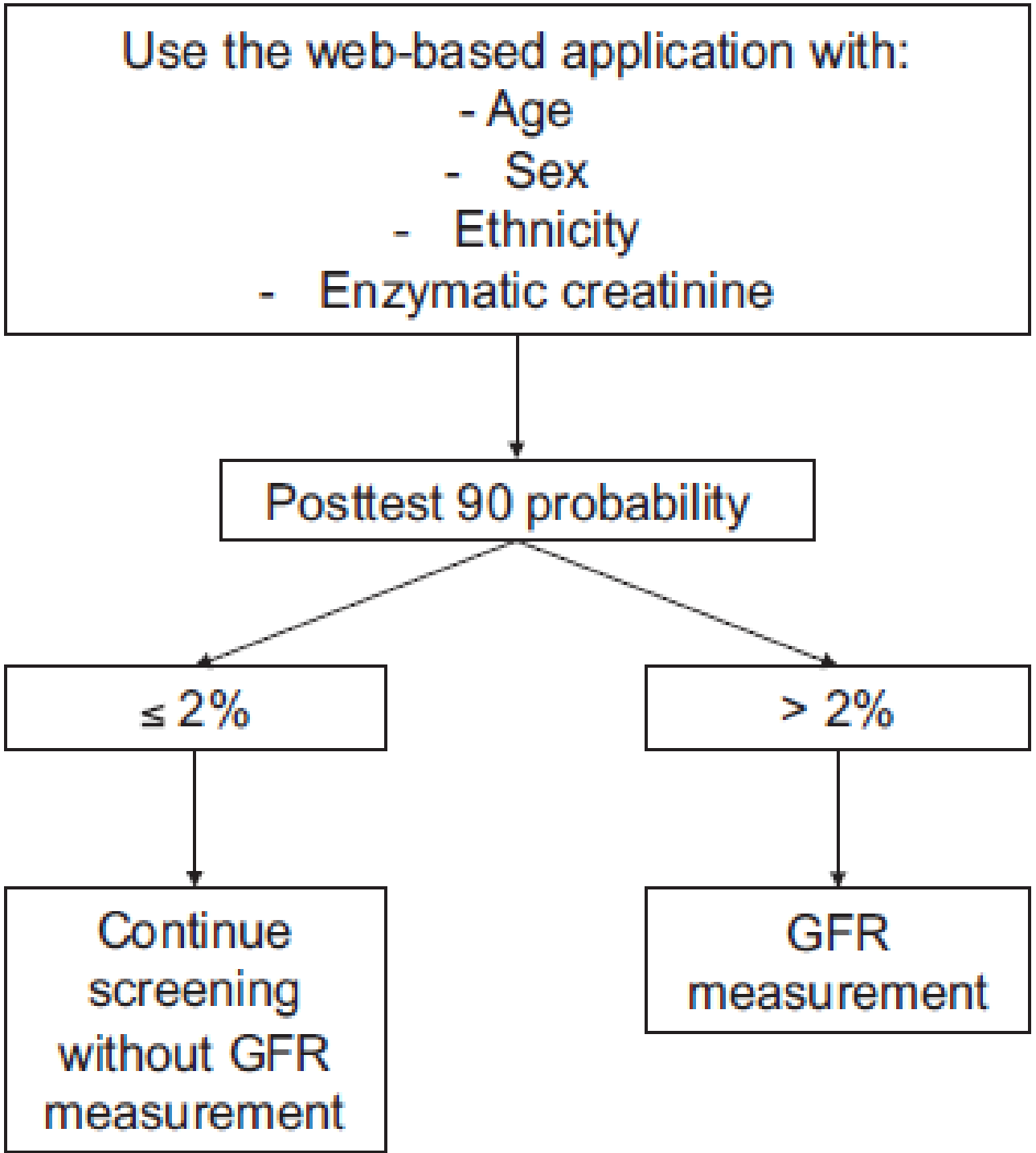
A recently published web-based application derived from large cohorts, but not living donors, calculates the probability of a measured GFR (mGFR) lower than a determined threshold. Our objectives were to validate the clinical utility of this tool in a cohort of living donors and to test two other strategies based on chronic kidney disease epidemiology collaboration (CKD-EPI) and on MDRD-eGFR. GFR was measured using ^{51}Cr- ethylene-diamine tetraacetic acid urinary clearance in 311 potential living kidney donors (178 women, mean age 50 ± 11.6 years). The web-based tool was used to predict those with mGFR < 80 mL/min/1.73 m^2. Inputs to the application were sex, age, ethnicity, and plasma creatinine. In our cohort, a web-based probability of mGFR <90 mL/min/1.73 m^2 higher than 2% had 100% sensitivity for detection of actual mGFR <80 mL/min/1.73 m^2. The positive predictive value was 0.19. A CKD-EPI-eGFR threshold of 104 mL/min/1.73 m^2 and an MDRD-eGFR threshold of 100 mL/min/1.73 m^2 had 100% sensitivity to detect donors with actual mGFR <80 mL/min/1.73 m^2. We obtained similar results in an external cohort of 354 living donors. We confirm the usefulness of the web-based application to identify potential donors who should benefit from GFR measurement.


Use the web-based application with:
- Age
- Sex
- Ethnicity
- Enzymatic creatinine
Posttest 90 probability
≤ 2%
> 2%
Continue screening without GFR measurement
GFR measurement

- **Significant reduction** of the **cost of screening** without hampering the **safety of the donors**

- Use of any one of the three strategies- **reduction by app 28% in the number of mGFR**

- Reduction **increased to nearly 45%** in the **external cohort**

- Group **requiring mGFR** had significantly **lower eGFR at 1 year**

- **eGFR at donation** might be an important **determinant** of eGFR **after donation**

Assessment of ESRD Risk

- **First estimate** the long-term risk of **ESRD in the absence of donation** using demographic and clinical characteristics of the donor.

- Grams et al. **developed a web-based calculator** to estimate the **15-year and lifetime risks** of ESRD **in the absence of kidney donation,** on the basis of donor's characteristics

Johns Hokpins University: ESRD Risk Tool for Kidney Donor Candidates, 2015. Available at: http://www.transplantmodels.com/esrdrisk/

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Kidney-Failure Risk Projection for the Living Kidney-Donor Candidate

Morgan E. Grams, M.D., Ph.D., Yingying Sang, M.S., Andrew S. Levey, M.D., Kunihiro Matsushita, M.D., Ph.D., Shoshana Ballew, Ph.D., Alex R. Chang, M.D., Eric K.H. Chow, M.Sc., Bertram L. Kasiske, M.D., Csaba P. Kovesdy, M.D., Girish N. Nadkarni, M.D., M.P.H., Varda Shalev, M.D., M.P.A., Dorry L. Segev, M.D., Ph.D., Josef Coresh, M.D., Ph.D., Krista L. Lentine, M.D., Ph.D., and Amit X. Garg, M.D., Ph.D., for the Chronic Kidney Disease Prognosis Consortium*

BACKGROUND

approach to donor selection, we developed a tool that simultaneously incorporates multiple health characteristics to estimate a person's probable long-term risk of ESRD if that person does not donate a kidney.

METHODS

We used risk associations from a meta-analysis of seven general population cohorts, calibrated to the population-level incidence of ESRD and mortality in the United States, to project the estimated long-term incidence of ESRD among persons who do not donate a kidney, according to 10 demographic and health characteristics. We then compared 15-year projections with the observed risk among 52,998 living kidney donors in the United States.

RESULTS

and 0.04% among white women. Risk projections were higher in the presence of a lower estimated glomerular filtration rate, higher albuminuria, hypertension, current or former smoking, diabetes, and obesity. In the model-based lifetime projections, the risk of ESRD was highest among persons in the youngest age group, particularly among young blacks. The 15-year observed risks after donation among kidney donors in the United States were 3.5 to 5.3 times as high as the projected risks in the absence of donation.

ESRD Risk Tool for Kidney Donor Candidates

Projected Incidence of End-Stage Renal Disease:	
0.04% Pre-Donation 15-Year*	**0.30%** Pre-Donation Lifetime*
? Post-Donation 15-Year**	? Post-Donation Lifetime**

blue: < 1%, **green:** 1-2%, **yellow:** 2-3%, **orange:** 3-5%, **red:** >5%

The pre-donation risks represent projections if a person does not donate a kidney. Details about estimating post-donation risk are provided below.

reset print summary

Patient Characteristics:

Age (18-80yrs)	40
Gender	Female
Race (White or Black)	White
eGFR (mL/min/1.73m²)	90
Systolic Blood Pressure (mmHg)	120
Hypertension Medication	No Medication
BMI (kg/m²)	25
Non-Insulin Dependent Diabetes	No Diabetes
Urine Albumin to Creatinine (mg/g) click on units to change between mg/g and mg/mmol	4
Smoking History	Non-Smoker

Nephrol Dial Transplant (2017) 32: 216–223
doi: 10.1093/ndt/gfw429

ndt
Nephrology Dialysis Transplantation

NDT Perspectives

Long-term risks of kidney living donation: review and position paper by the ERA-EDTA DESCARTES working group

Umberto Maggiore[1], Klemens Budde[2], Uwe Heemann[3], Luuk Hilbrands[4], Rainer Oberbauer[5], Gabriel C. Oniscu[6], Julio Pascual[7], Soren Schwartz Sorensen[8], Ondrej Viklicky[9] and Daniel Abramowicz[10] for the ERA-EDTA DESCARTES working group

[1]Department of Nephrology, Azienda Ospedaliero-Universitaria di Parma, Parma, Italy, [2]Department of Nephrology, Charité Medical University Berlin, Berlin, Germany, [3]Department of Nephrology, Technical University of Munich, Munich, Germany, [4]Department of Nephrology, Radboud University Medical Centre, Nijmegen, The Netherlands, [5]Department of Nephrology, Medical University of Vienna, Vienna, Austria,

- The predicted **pre-donation risk** for **ESRD** is **0.10% after 15 years**.

- It is likely that, on average, the ESRD risk is **increased by nephrectomy by 3–5 times or by 0.30% absolute risk** 15 years after donation (e.g. from 0.10 to 0.40%, which is well below an absolute risk of 1% despite donor nephrectomy)

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NDT Perspectives

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Umberto Maggiore[1], Klemens Budde[2], Uwe Heemann[3], Luuk Hilbrands[4], Rainer Oberbauer[5], Gabriel C. Oniscu[6], Julio Pascual[7], Soren Schwartz Sorensen[8], Ondrej Viklicky[9] and Daniel Abramowicz[10] for the ERA-EDTA DESCARTES working group

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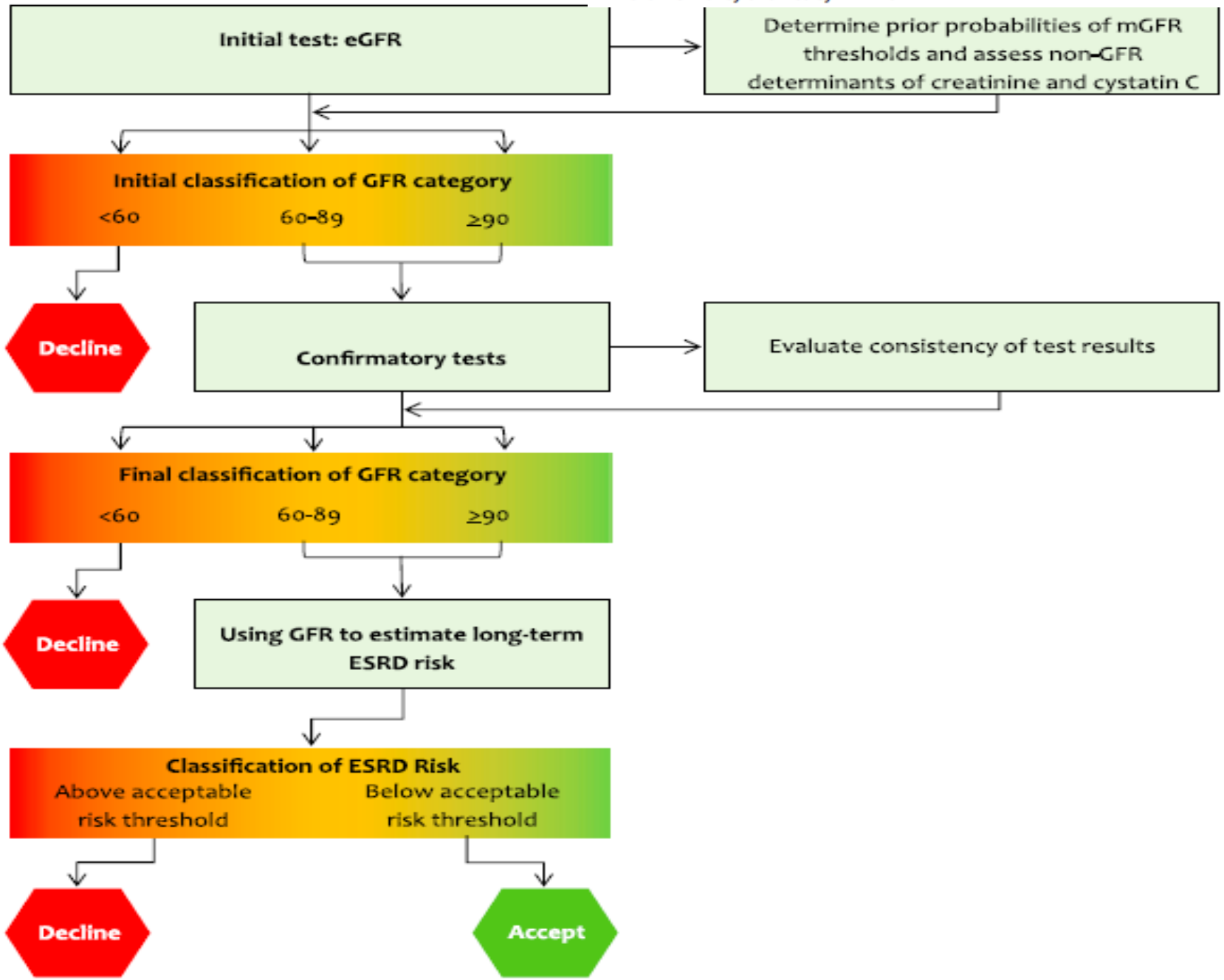
- The prediction model for lifetime risk is **based on a simulation** study

- It **does not** take into **account** a **family history** of **renal disease** which is **the most important ESRD risk indicator in young donors** with normal workup at evaluation

GFR Evaluation in Living Kidney Donor Candidates

J Am Soc Nephrol 28: ••• •••, 2017.

Andrew S. Levey and Lesley A. Inker



Renal Function Profile in White Kidney Donors: The First 4 Decades

Hassan N. Ibrahim,* Robert N. Foley,* Scott A. Reule,* Richard Spong,* Aleksandra Kukla,* Naim Issa,* Danielle M. Berglund,† Gretchen K. Sieger,† and Arthur J. Matas†

*Division of Renal Diseases and Hypertension, and †Department of Surgery, University of Minnesota, Minneapolis, Minnesota

ABSTRACT

Previous studies reported the risk of ESRD after kidney donation, but not the renal outcomes that precede ESRD. Here, we estimated the risk of proteinuria, reduced GFR, and ESRD in 3956 white kidney donors, assessed the contribution of postdonation hypertension and diabetes to these outcomes, and developed a risk calculator. After a mean±SD follow-up of 16.6±11.9 years, 215 (6.1%) donors developed proteinuria. Men had a higher risk of proteinuria (hazard ratio [HR], 1.56; 95% confidence interval [95% CI], 1.18 to 2.05; $P<0.001$) as did those with higher body mass index (HR, 1.10; 95% CI, 1.06 to 1.13; $P<0.001$). In all, 1410 (36%) donors reached an eGFR<60 ml/min per 1.73 m^2, and 112 (2.8%) donors had either an eGFR<30 ml/min per 1.73 m^2 or ESRD (28 donors developed ESRD). An eGFR<30 ml/min per 1.73 m^2 or ESRD associated with older age (HR, 1.07; 95% CI, 1.05 to 1.09; $P<0.001$), higher body mass index (HR, 1.08; 95% CI, 1.04 to 1.13; $P<0.001$), and higher systolic BP (HR, 1.02; 95% CI, 1.00 to 1.04; $P=0.01$) at donation. Postdonation diabetes and hypertension associated with a fourfold higher risk of proteinuria and a >2-fold higher risk of ESRD. Models predicting proteinuria and reduced eGFR performed well (C-index 0.77–1.00). In conclusion, severe reduction in GFR and ESRD after kidney donation were uncommon and were highly associated with postdonation diabetes and hypertension. Furthermore, information available before donation may predict long-term renal outcomes in white living kidney donors.

J Am Soc Nephrol 27: ●●●–●●●, 2016. doi: 10.1681/ASN.2015091018

Nephrol Dial Transplant (2017) 32: 216–223
doi: 10.1093/ndt/gfw429

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Nephrology Dialysis Transplantation

NDT Perspectives

Long-term risks of kidney living donation: review and position paper by the ERA-EDTA DESCARTES working group

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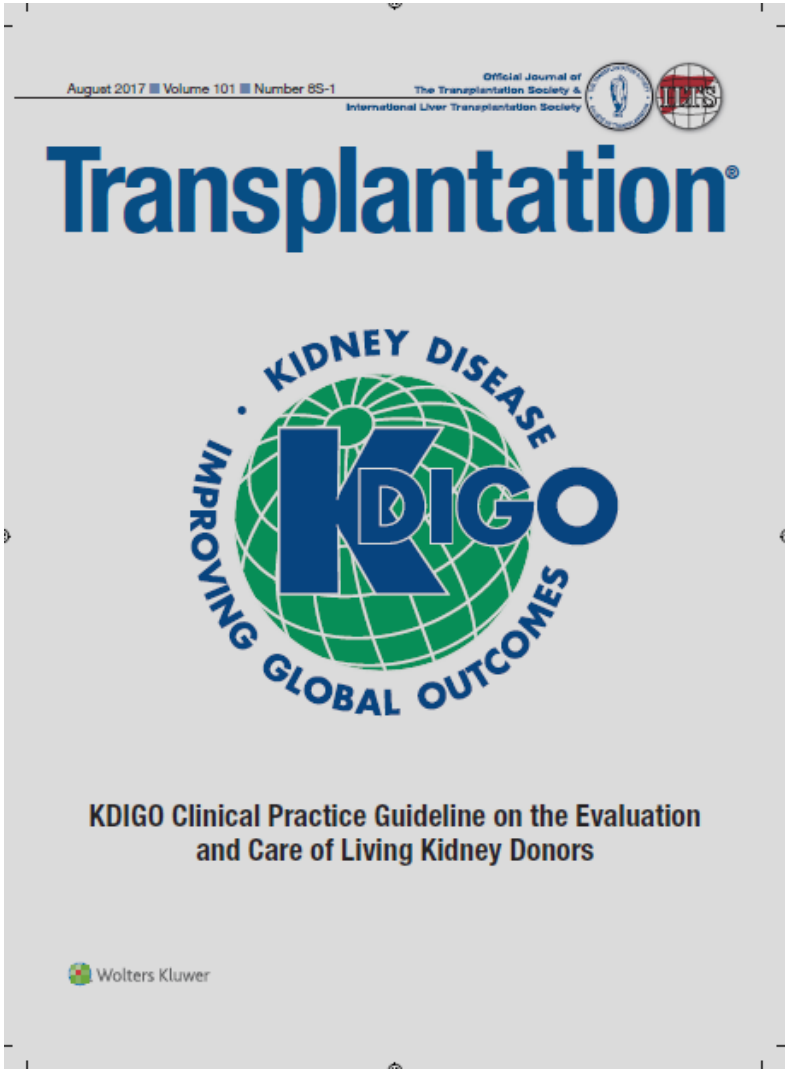
- All transplant teams should make every possible effort to **help prospective donors** make an informed decision by **providing** them with **quantitative risk estimates.**

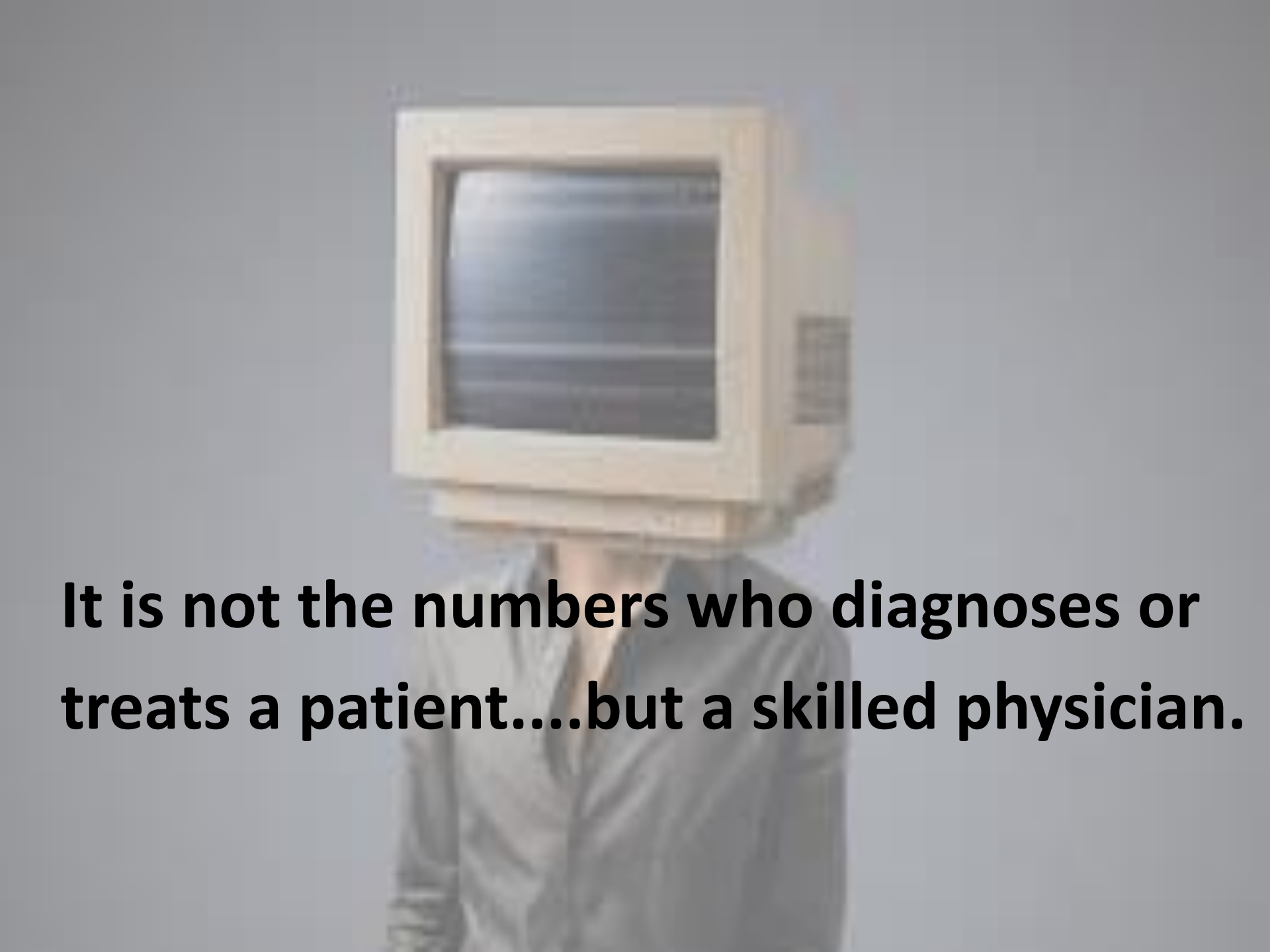
- Physicians should **recognize** that **donors** may also **benefit**, which adds **another perspective** for justifying living organ donation.

- **Proper information** to the prospective donor should **also include** recommendations on health-promoting **behaviour post-donation**



- **Quantifying donation**-attributable **relative risk** for a given clinical profile and **incorporating** updated **estimates into the online tool** should be a leading priority for **future research.**

- Use of such **tools require clinician insight**, and transplant centers and donor candidates may **consider other factors** in their acceptance criteria for living kidney donation **in addition to quantitative risk estimates**.



It is not the numbers who diagnoses or treats a patient....but a skilled physician.