The Science of Stewardship: Due Diligence for Kidney Donors and Kidney Function in Living Kidney Donation—Evaluation, Determinants, and Implications for Outcomes

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Living kidney donor transplantation is now a common treatment for ESRD because it provides excellent outcomes to transplant recipients and is considered a safe procedure for prospective donors. The short- and long-term safety of prospective donors is paramount to the continued success of this procedure. Whereas the initial experiences with living kidney donors mostly included the healthiest, the increase in the need for organs and the changing demographic characteristics of the general population have subtly reshaped the suitability for donation. Kidney function assessment is a critical component of the evaluation of prospective donors; therefore, special emphasis is usually placed on this aspect of the evaluation. At the same time, consideration of kidney function after donation is important because it assists with the determination of renal health in donors. This review summarizes the process of predonation kidney function assessment, determinants of pre- and postdonation renal function, and, importantly, the potential implications of kidney function to the long-term outcomes of kidney donors.

Kidney transplantation is considered the best treatment for patients with ESRD (1). Living kidney donation not only allows for a planned transplantation process but also provides better clinical outcomes when compared with those of deceased donors. The continuously increasing demand for organs and the changing demographics of the living kidney donor population have been subtly reshaping concepts of suitability for donation, including levels of renal function, with less strict clinical criteria of acceptance (1–5).

Three current issues for living donors are their increasing age at donation, selected acceptance with isolated medical abnormalities, and renal function outcomes and consequences that may include chronic kidney disease (CKD) (6). The proportion of donors aged ≥50 yr at time of donation has nearly doubled in the past 20 years (3,4). Furthermore, some renal transplantation programs have begun to allow selected individuals with hypertension to donate a kidney (7). Accurate assessment of kidney function and an appropriate threshold for acceptance of a donor are essential in these cases, as will be long-term functional outcomes. The unintended consequence of living kidney donation could be development of stage 3 CKD according to current recommendations for staging of kidney disease by the National Kidney Foundation (NKF) (8,9); however, the correct interpretation of this staging for former living donors is being challenged (10–14).

Unique to the practice of medicine, living kidney donors undergo extensive evaluation with the central goal of confirming suspected health instead of suspected disease. Because kidney donation is an elective procedure with no direct physical benefit to the donor, it is essential that the evaluation process carefully assess predonation kidney function and put into perspective the factors that may potentially affect postnephrectomy GFR. Interpreting whether predonation GFR will adequately provide enough residual postnephrectomy GFR to the donor and sufficient GFR to the recipient is crucial to a successful transplant procedure. According to current recommendations, living donors should have a GFR of ≥80 ml/min or, alternatively, a kidney function level within 2 SD of normal for age and gender (2–5). These recommendations do not clearly specify the method for renal function assessment; however, most centers perform this critical step using timed urine collections for creatinine clearance. Others rely on more precise and accurate techniques, such as exogenous marker clearances. Nevertheless, no standardized reference values exist for each of the procedures used in clinical practice. Thus, the decision of proceeding (or not) with donation is often left to subjective interpretation. Because of the emphasis placed by the NKF on GFR to determine the state of renal health versus disease, a comprehensive exposition of kidney function and its determinants is presented herein through the entire process of living kidney donation, from the initial prenephrectomy evaluation to long-term postdonation GFR assessment.
Predonation Evaluation of Kidney Function

Traditionally, GFR has been considered the best overall marker of kidney function (15). In clinical practice other than living kidney donor evaluation, GFR is commonly inferred by either the interpretation of serum creatinine levels or, since the advent of the Kidney Disease Outcomes Quality Initiative (K/DOQI) guidelines, by the use of creatinine-based GFR estimation equations such as the Modification of Diet in Renal Disease (MDRD) equation (8,16). Although the use of serum creatinine alone has numerous limitations, its main benefit is its relative ease of use and wide availability. Nevertheless, it is clear that this approach is not acceptable in the setting of living donor evaluation mostly because a significant percentage of kidney function may have to be lost before there is an overtly abnormal serum creatinine level. However, although serum creatinine is not a sensitive marker of kidney dysfunction, it is a specific marker of kidney disease (17). For example, if a prospective donor has a serum creatinine level above normal values during the evaluation process, then the donor is likely to have kidney disease and therefore this approach could be used for initial screening of interested prospective donors.

During the past decade, significant advances have been made in the estimation of GFR with the introduction of the MDRD equation (16). In the setting of established kidney disease, the MDRD equation is an optimal tool to estimate the degree of kidney dysfunction; however, the shortcomings are evident when used to assess predonation GFR (18–20). In the state of health such as living donation, estimation of GFR from creatinine-based estimation equations underestimates the measured GFR. Furthermore, it is not a sensitive marker to detect kidney dysfunction (18), and, when abnormal, it does not provide any more diagnostic information than an elevated creatinine alone (17). A new creatinine-based GFR estimation equation aimed at improving its performance in the setting of health was recently presented by the CKD-EPI Study Group (21); however, external validation of this model to support its clinical application in prospective kidney donors has not yet been attempted.

The urine creatinine clearance has traditionally been the method of choice to study kidney function in potential donors. Two clearances are usually done to minimize the potential for methodologic limitations, a common problem with this method. Although the creatinine clearance always overestimates true GFR because of the universal tubular secretion of creatinine, in conjunction with a comprehensive laboratory and medical evaluation, this method has become the “standard of care” by transplant centers mostly because of the lack of a better alternative. Nevertheless, in one study, the performance of creatinine clearance against the gold standard was not only poor but even worse than that of serum creatinine–based methods when compared with radioisotope urinary clearances (22). Use of creatinine clearance in prospective living donors has major potential deficiencies: (1) It is reliable only when done properly but still has significant variability, (2) it overestimates GFR by a nonconstant and therefore unpredictable percentage, and (3) it is not usually interpreted with necessary age- and gender-specific reference values. To exemplify each of these points, consider a potential kidney donor who has two urinary clearances of creatinine (point 1) that average 87 ml/min and allow donation. This average value may actually reflect a GFR of <80 ml/min per 1.73 m² (point 2). Moreover, although this value may be normal for a 55-yr-old female donor, it may not be for a 25-yr-old male donor (point 3); therefore, extreme caution should be used with this assessment approach.

Assessment of GFR by clearances of exogenous markers has become the “gold standard” approach. Their use in living kidney donors could be considered one of the most clinically valuable applications of these methods. Clearance techniques using various radioactive (“hot”) and nonradioactive (“cold”) markers have emerged (23,24). Although these methods are also not exempt from methodologic variability, they are more consistent and reliable. Currently, donor renal function is often evaluated without consideration of age- and gender-specific reference values with the result that any value >80 ml/min per 1.73 m² is in general considered appropriate for proceeding with donation. Although long-term follow-up has demonstrated that former kidney donors have similar or better life expectancy and lower risk for ESRD than the general population (25–27), a small number of kidney donors have developed the need for renal replacement therapy (28). This outcome might be unavoidable in some because of new and unpredictable kidney disease, but it is not clear whether individuals with prenephrectomy GFR >80 ml/min per 1.73 m² but in the lower percentiles of normal on the basis of age and gender reference values (i.e., abnormal or suboptimal) are a higher risk for poor renal outcomes. In fact, the subpopulation at highest risk may be young donors, in whom the lowest normal values are commonly >80 ml/min per 1.73 m², (19,20) but who are young enough to develop kidney disease during their lifetime in contrast to older donors with no identified medical conditions during donor evaluation.

Postnephrectomy GFR and Determinants of Reserve Capacity and Residual Kidney Function

Donor nephrectomy represents the sudden loss of approximately 50% of nephron mass with an immediate and corresponding decrease in GFR; however, the remaining contralateral healthy renal parenchyma has the ability to recover a significant percentage of lost function within a relatively short period. Since the early years of kidney donation, several investigators have shown that in healthy individuals, unilateral nephrectomy is followed by a compensatory increase in functional capacity of the contralateral kidney by approximately 20 to 40% (Table 1) (29–32). Velosa et al. (32), among others, showed that as early as 1 wk after nephrectomy, renal function has recovered to levels slightly lower than those achieved at 6 mo after nephrectomy. Similarly, others showed that the GFR at 1 yr after donation was essentially the same as the one achieved as early as 1 wk after donation (29,33).

The mechanisms of this “adaptive hyperfiltration” are complex and determined by several factors (31). Demographic factors may be important in the potential for GFR compensation after nephrectomy and include age, gender, race, and body size.
Table 1. Studies in which pre- and postdonation GFR was studied by exogenous marker clearances

<table>
<thead>
<tr>
<th>Study</th>
<th>No. and Type of Patients</th>
<th>Method of GFR Testing</th>
<th>Nonstimulated Basal GFR (ml/min per 1.73 m²; Mean)</th>
<th>Stimulated Basal GFR</th>
<th>Postnephrectomy GFR</th>
<th>Time Postnephrectomy GFR</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Absolute (ml/min per 1.73 m²; Mean)</td>
<td>% Change from Baseline</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Absolute (ml/min per 1.73 m²; Mean)</td>
<td>% Changea</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fliser et al. (52), 1993</td>
<td>15 young</td>
<td>Inulin</td>
<td>122</td>
<td>146</td>
<td>16</td>
<td>NA</td>
</tr>
<tr>
<td></td>
<td>10 elderly</td>
<td>Inulin</td>
<td>102</td>
<td>118</td>
<td>17</td>
<td>NA</td>
</tr>
<tr>
<td>Rook et al. (53), 2006</td>
<td>125 donors</td>
<td>Iothalamate</td>
<td>104</td>
<td>143</td>
<td>38</td>
<td>66</td>
</tr>
<tr>
<td>Rook et al. (37), 2008</td>
<td>178 donors</td>
<td>Iothalamate</td>
<td>114</td>
<td>126</td>
<td>10</td>
<td>73</td>
</tr>
<tr>
<td>Faluno et al. (39), 2001</td>
<td>10 young</td>
<td>Inulin</td>
<td>127</td>
<td>167</td>
<td>31</td>
<td>NA</td>
</tr>
<tr>
<td></td>
<td>11 elderly</td>
<td>Inulin</td>
<td>79</td>
<td>94</td>
<td>19</td>
<td>NA</td>
</tr>
<tr>
<td>Barai et al. (41), 2008</td>
<td>109 donors</td>
<td>Iothalamate</td>
<td>82</td>
<td>105</td>
<td>27</td>
<td>NA</td>
</tr>
<tr>
<td></td>
<td>6 subjects</td>
<td>Iothalamate</td>
<td>114</td>
<td>129</td>
<td>13</td>
<td>NA</td>
</tr>
<tr>
<td>Englert et al. (55), 1997</td>
<td>15 donors</td>
<td>Inulin</td>
<td>79</td>
<td>106</td>
<td>34</td>
<td>NA</td>
</tr>
<tr>
<td>de Santo et al. (56), 1997</td>
<td>10 healthy subjects</td>
<td>Inulin</td>
<td>99</td>
<td>125</td>
<td>27</td>
<td>NA</td>
</tr>
<tr>
<td>Sackmann, et al. (57), 1998</td>
<td>12 healthy subjects</td>
<td>Inulin</td>
<td>113</td>
<td>142</td>
<td>26</td>
<td>NA</td>
</tr>
<tr>
<td>George et al. (58), 1996</td>
<td>9 healthy subjects</td>
<td>⁹⁹ᵐTc-DTPA</td>
<td>91</td>
<td>NA</td>
<td>NA</td>
<td>56</td>
</tr>
<tr>
<td>Fliser et al. (59), 1995</td>
<td>12 healthy subjects</td>
<td>Inulin</td>
<td>113</td>
<td>142</td>
<td>26</td>
<td>NA</td>
</tr>
<tr>
<td>Bock et al. (33), 1992</td>
<td>30 donors</td>
<td>Inulin</td>
<td>104</td>
<td>NA</td>
<td>NA</td>
<td>66</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bohlin and Berg (60), 1991</td>
<td>19 donors</td>
<td>Inulin</td>
<td>68</td>
<td>NA</td>
<td>NA</td>
<td>Not given</td>
</tr>
<tr>
<td>ter Wee et al. (61), 1990</td>
<td>20 donors</td>
<td>Iothalamate</td>
<td>107</td>
<td>132</td>
<td>23</td>
<td>69</td>
</tr>
<tr>
<td>Pabico et al. (62), 1975</td>
<td>7 donors</td>
<td>Inulin</td>
<td>110</td>
<td>NA</td>
<td>NA</td>
<td>76</td>
</tr>
<tr>
<td>Ewald and Aurell (63), 1975</td>
<td>9 donors</td>
<td>Inulin</td>
<td>105</td>
<td>NA</td>
<td>NA</td>
<td>67</td>
</tr>
<tr>
<td>Skov and Hansen (64), 1974</td>
<td>13 donors</td>
<td>Inulin and iothalamate</td>
<td>92</td>
<td>NA</td>
<td>NA</td>
<td>78</td>
</tr>
<tr>
<td>Boner et al. (29), 1973</td>
<td>49 donors</td>
<td>Inulin and iothalamate</td>
<td>111</td>
<td>NA</td>
<td>NA</td>
<td>7</td>
</tr>
<tr>
<td>Velosa et al. (32), 1995</td>
<td>105 young donors</td>
<td>Inulin or iothalamate</td>
<td>113</td>
<td>NA</td>
<td>NA</td>
<td>76</td>
</tr>
<tr>
<td></td>
<td>35 elderly donors</td>
<td>Inulin or iothalamate</td>
<td>88</td>
<td>NA</td>
<td>NA</td>
<td>55</td>
</tr>
</tbody>
</table>

aIn relation to 50% of baseline prenephrectomy GFR
The relationship between GFR and aging has been a matter of investigation for decades. Although an invariable decrement in GFR occurs as humans age, when this physiologic process becomes a pathologic one is debatable (20,31,34–36). Moreover, it seems that the GFR decline with aging, although continuous, is not constant (34,36). Rule et al. (19) reported that GFR decreases at a rate of approximately 4 ml/min per 1.73 m² per decade of life. A recent larger study by Poggio et al. (20) of 1015 donors showed that GFR declines faster as individuals age. In that study, the decline in GFR was approximately 4 ml/min per 1.73 m² per decade of life for donors who were younger than 45 yr; however, the rate of GFR decline for individuals who were older than 45 yr increased to approximately 8 ml/min per 1.73 m². Several investigators hypothesized that kidneys from older donors would have a decreased “renal reserve capacity” that would manifest as impaired kidney function after donation. Studies by Velosa et al. as well as by Saxena et al., among others, showed that although aging individuals have a lower absolute baseline GFR, they do not necessarily lose the adaptive hyperfiltration capability that is observed after nephrectomy when compared with younger donors. Furthermore, postnephrectomy GFR seems to depend mostly on the prenephrectomy GFR (31,32). Using a different approach, Rook et al. (37,53) reported that although the postnephrectomy GFR may not be affected by age, the postnephrectomy reserve capacity of the remaining kidney as assessed by amino acid–induced hyperfiltration was significantly impaired in older and heavier donors. Reported ranges of induced renal hyperfiltration in non-nephrectomized healthy individuals vary between 20 and 35% of basal of nonstimulated GFR (Table 1). Humans may lose renal reserve as they age because of nephron loss possibly secondary to glomerulosclerosis and/or renal microvascular disease (39). Although these processes are nonphysiologic, they seem to be prevalent in the aging population that includes living kidney donors.

Obesity is a current major health care concern in most Western societies, and current donors are also becoming “victims” of this epidemic. The impact of obesity on GFR deserves attention. In a recent analysis of GFR measurements performed over three decades, we showed that donors were 3.38 yr older and had a 0.88-kg/m² greater body mass index per decade of evaluation from 1972 to 2005. Importantly, because GFR unadjusted for body size remained constant during 33 yr in this cohort, use of an adjustment for body surface area (which increased over time) translated into a loss of 1.49 ml/min per 1.73 m² of corrected GFR per decade of testing and almost a 5-ml/min per 1.73 m² of mean GFR “loss” during the study period (20). Rook et al. (37) studied how age and body size affected renal reserve capacity after donor nephrectomy. These investigators showed that reserve capacity was preserved independent of body mass index before donation, but after donation, it was blunted in overweight and obese donors. Similar findings were reported when the studied cohort was assessed on the basis of age. When these two variables were analyzed together, younger overweight donors seemed to be the most likely to lack reserve capacity after donation. Whether reserve capacity after donation is a surrogate marker of long-term risk for suboptimal kidney function is unknown, but caution should be used when evaluating young obese donors who still have decades to live and the potential to develop kidney disease.

Finally, because of the wider acceptance of living donation among various races and cultures, the current living donor population is also becoming more multiracial. The effects of race on GFR are not clear because most reports described white populations. In our own experience, black individuals have comparable levels of GFR and age-associated rates of GFR decline when compared with non-black individuals (20). Donors of Indian background have lower levels of GFR, but they maintain induced hyperfiltration rates similar to those observed in white individuals (40–42). Further studies of kidney function in prospective kidney donors of other minorities and races are needed. Gender does not seem to be a determinant factor of pre- and postnephrectomy GFR, but women are more likely to have lower GFR after donation, possibly as a consequence of having normally lower predonation GFR levels compared with men. Moreover, women are more likely to have less albuminuria despite a lower GFR when compared with men after donation (27).

Long-Term Renal Outcomes and Implications for Subsequent Kidney Disease

During the past decade, the NKF provided the framework for a new approach to the diagnosis, staging, and management of kidney disease. Estimation of GFR plays a pivotal role in not only defining but also classifying kidney disease; however, the definition of kidney disease does not take into consideration the underlying pathologic process that determines the degree of kidney dysfunction. Therefore, evidence of parenchymal kidney damage is not required to establish the diagnosis of stage 3 CKD as long as the estimated GFR is <60 ml/min per 1.72 m², a level that could be seen in former donors. Justification for using this cutoff value as the sole driver in establishing CKD is extracted from epidemiologic data associating low GFR with increased cardiovascular and overall mortality (43). Whether an isolated decreased GFR in an otherwise healthy individual (e.g., former kidney donors) should be considered “chronic disease” remains a matter of debate (10). The question that the transplant community now faces is whether the current approach to CKD is applicable to living kidney donors. Prospective studies to address this matter specifically are not available yet, although single-center experiences with long-term follow-up indirectly provide reassuring results.

First, the current diagnosis and classification of CKD require that GFR be estimated (16). Available models to estimate GFR (e.g., MDRD equation) have been developed from patients with established CKD; that is, individuals with an underlying renal pathologic process. Kidney donors who are specifically evaluated to exclude any such pathologic process but now have just a single kidney could have estimated GFR levels <60 ml/min per 1.73 m², a level at which the MDRD equation improves its performance. Studies that used the MDRD equation found that the prevalence of CKD was common in kidney donors on the basis of GFR estimations; however, the GFR was indeed higher when measured by an endogenous marker (44,45). Misdiagno-
Table 2. Studies that reported on long-term clinical and mortality outcomes after living kidney donation

<table>
<thead>
<tr>
<th>Study</th>
<th>Years of Donation</th>
<th>No. of Donors</th>
<th>Lost to Follow-up/Unknown/Other</th>
<th>Available for Analysis</th>
<th>Age at Donation (yr)</th>
<th>Kidney Function at Follow-up</th>
<th>Proteinuria</th>
<th>Hypertension (%)</th>
<th>ESRD</th>
<th>Dead</th>
</tr>
</thead>
<tbody>
<tr>
<td>Najarian et al. (65), 1992</td>
<td>1963 to 1970</td>
<td>135</td>
<td>57</td>
<td>78</td>
<td>43</td>
<td>82 ml/min by CrCl</td>
<td>23% with &gt;0.15 g/d</td>
<td>32</td>
<td>Not stated</td>
<td>15</td>
</tr>
<tr>
<td>Fehrman-Ekholm et al. (25), 1997</td>
<td>1964 to 1994</td>
<td>459</td>
<td>29</td>
<td>430</td>
<td>80% with SCr within normal limits, 20% with elevated SCr</td>
<td>20%</td>
<td>35</td>
<td>41</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fehrman-Ekholm et al. (46), 2001</td>
<td>1964 to 1995</td>
<td>451</td>
<td>97</td>
<td>348</td>
<td>49</td>
<td>Mean SCr 1.16 mg/dL, eGFR 72% of predonation GFR</td>
<td>12% with &gt;0.30 g/d</td>
<td>38</td>
<td>1</td>
<td>49</td>
</tr>
<tr>
<td>Goldfarb et al. (66), 2001</td>
<td>1963 to 1975</td>
<td>180</td>
<td>110</td>
<td>70</td>
<td>40</td>
<td>73 ml/min by CrCl, 72% of predonation GFR</td>
<td>19% with &gt;0.15 g/d and 38% with albumin &gt;10 μg/min</td>
<td>48</td>
<td>2</td>
<td>24</td>
</tr>
<tr>
<td>Ellison et al. (28), 2002</td>
<td>UNOS registry up to 2002</td>
<td>NA</td>
<td>NA</td>
<td>56</td>
<td>31</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>56</td>
<td>NA</td>
</tr>
<tr>
<td>Gessmann et al. (47), 2005</td>
<td>1973 to 2001</td>
<td>152</td>
<td>10</td>
<td>135</td>
<td>45</td>
<td>99 ml/min by CrCl</td>
<td>56% with &gt;0.15 g/d and 10% with albumin &gt;30 mg/L</td>
<td>30</td>
<td>0</td>
<td>7</td>
</tr>
<tr>
<td>Gibney et al. (67), 2007</td>
<td>UNOS data 1993-2003</td>
<td>62,327</td>
<td>NA</td>
<td>102</td>
<td>32</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>102</td>
<td>NA</td>
</tr>
<tr>
<td>Gibney et al. (49), 2008</td>
<td>UNOS data 1988 to 2006</td>
<td>78,609</td>
<td>NA</td>
<td>126</td>
<td>31</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>126</td>
<td>NA</td>
</tr>
<tr>
<td>Ibrahim et al. (27), 2009</td>
<td>1963 to 2007</td>
<td>3698</td>
<td>26</td>
<td>3404F</td>
<td>41</td>
<td>64 ml/min per 1.73 m² by MDRD equation and 76 ml/min per 1.73 m² by iohexol urinary clearance</td>
<td>11.5% with microalbuminuria and 1.2% with macroalbuminuria</td>
<td>32</td>
<td>11</td>
<td>268</td>
</tr>
<tr>
<td>Okamoto et al. (68), 2009</td>
<td>1972 to 2006</td>
<td>601</td>
<td>120</td>
<td>426</td>
<td>NA</td>
<td>NA</td>
<td>9.4% reported to have &quot;renal problems,&quot; not ESRD</td>
<td>30.1</td>
<td>4</td>
<td>55</td>
</tr>
</tbody>
</table>

CrCl, creatinine clearance; eGFR, estimated GFR; SCr, serum creatinine; UNOS, United Network for Organ Sharing.

aSimilar data set to the one used in article by same author from 1997 (25).
bSimilar data set to the one used in article by same author from 2007 (67).
cA total of 255 donors were available for clinical follow-up.
sis of CKD by the use of the MDRD equation (as a result of underestimation of GFR) is likely explained by the fact that current estimation equations do not model the biologic relationships between creatinine and demographics in kidney donors without kidney disease. The clinical applicability of this approach to establish CKD versus nondisease remains unknown. Similarly, it is unclear whether microalbuminuria in this population has any clinical relevance. In a large cohort of kidney donors who were followed for approximately four decades, Ibrahim et al. (27) reported that <15% of donors had a measured GFR by iohexol clearance of <60 ml/min per 1.73 m², and none had a GFR of <30 ml/min per 1.73 m². The rate of decline of GFR after donation remained within the expected values observed in healthy individuals with two functional kidneys, suggesting that there was no added underlying pathophysiologic process other than those observed with aging alone (18,20,27,46). In that same study, approximately 13% of kidney donors had some degrees of microalbuminuria, but none of the patients had both decreased GFR and albuminuria, again suggesting that these observations in isolation may not necessarily represent kidney disease in this population; however, the study population was mostly white, and, thus, these findings would need to be validated in a wider population of donors.

Perhaps more important is whether any decrease in GFR (with or without albuminuria) has a negative impact on the long-term quality and extent of life after donation—outcomes that are considered by the NKF to justify the applicability of current guidelines for CKD. Although there have been reports of the need for renal replacement therapy in kidney donors, the preponderance of evidence continues to indicate that kidney donors live at least as long as the general population (25,27,28,46–49). Despite the fact that mild hypertension, decreased GFR, and low levels of proteinuria are commonly reported in these cohorts (50), the rates of ESRD and/or mortality are similar or lower than what is expected in the general population (Table 2). Some have hypothesized that the outcomes in donors should be better than those in the general population because the latter includes individuals with undiagnosed medical and renal disease; however, this opinion may be debatable, because although donors are screened for disease before donation, they are not exempt from developing medical conditions after donation. Causes of death seem to be similar to those observed in the general population, with cardiovascular events and malignancies being the most frequently reported. Factors that were found to be associated with renal dysfunction, albuminuria, and/or hypertension are time since transplantation (i.e., younger donors), female gender, and increased body weight in one study (27); however, in a study using the United Network for Organ Sharing registry, young male black donors had a higher risk for needing kidney transplantation (49). Finally, in the few studies in which quality of life was assessed, former donors reported superior scores when compared with those observed in the general population (27,51).

Conclusions
There is a need for continuing emphasis on accurate evaluation of kidney function in prospective and previous living donors. Factors such as donor age, weight, and race may be relevant to the long-term safety of donors. Future guidelines should incorporate these factors when interpreting predonation GFR values rather than focusing on a single unreferenced cutoff value (currently 80 ml/min) that could lead to underappreciation of renal dysfunction. Common conditions that cause renal and cardiovascular disease will become increasingly important to quantify in the current era of changing demographics to continue protecting living kidney donors and making living kidney donation the success it has been for almost six decades.

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Disclosures
None.

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