LIVING KIDNEY DONATION: ALTRUISM AT ITS FINEST….BUT WHAT ARE THE RISKS?

Swee-Ling Levea, M.D.
Division of Nephrology
Transplant Nephrology
University of Texas Southwestern Medical Center
Internal Medicine Grand Rounds
January 6, 2017

This is to acknowledge that Swee-Ling Levea, M.D. has disclosed that she does not have any financial interests or other relationships with commercial concerns related directly or indirectly to this program. Dr. Levea will not be discussing off-label uses in her presentation.

Name: Swee-Ling Levea, M.D.

Academic Rank: Assistant Professor

Division: Nephrology, Transplant Nephrology

Dr. Levea is originally from Malaysia and grew up in Austin, Texas. She received her undergraduate degree from University of Texas, Austin and her medical degree from University of Texas Health Science Center – San Antonio. After residency at Cleveland Clinic Foundation, she moved to Vanderbilt University and completed fellowships in nephrology and transplant nephrology, where she also served as a chief fellow. Her clinical interest is in living kidney donation with focus on donor education and long-term outcomes of prior kidney donors.

Purpose and Overview
Living kidney donation benefits recipients but carries short term and long term risks for the donor. This talk will summarize the current understanding of these risks and provides a perspective regarding long-term management of these kidney donor.

Educational Objectives:

1. Understand the evaluation of a potential living donor.
2. Understand the long-term renal risk and pregnancy risk after donation.
3. Understand the long-term risk with donation from a medically complex donor.
4. Impact of ethnicity on medical outcomes and renal risk after donation.
5. Long-term management of prior living kidney donors.

INTRODUCTION

The number of patients with end-stage renal disease (ESRD) has steadily increased in the last decade with close to 120,000 individuals on dialysis. With that, there is a similar increase in the number of individuals awaiting kidney transplantation with close to 100,000 individuals on the waitlist in the United States.[1] However, there is a significant organ shortage in the United States with minimal expansions of the deceased donor pool. Living kidney donation provides an ability to expand the donor pool. Living donation is also associated with better long-term allograft and recipient survival.

The first successful living donor kidney transplantation was performed on December 23rd, 1954 between identical twins, Ronald and Richard Herrick in Brigham's and Women's Hospital in Boston, Massachusetts. Since then, more than a half million living donor transplantations have been performed worldwide, with 5,000-6,000 performed annually in the United States alone.

TYPES OF LIVING DONATION

Directed donation

In this setting, the donor names the specific person to receive the transplant. This can be either from a biological relative (living related) or biologically unrelated individual (living unrelated) who has a personal or social connection with the transplant candidate. Living unrelated donation is now the most common type of living donation.

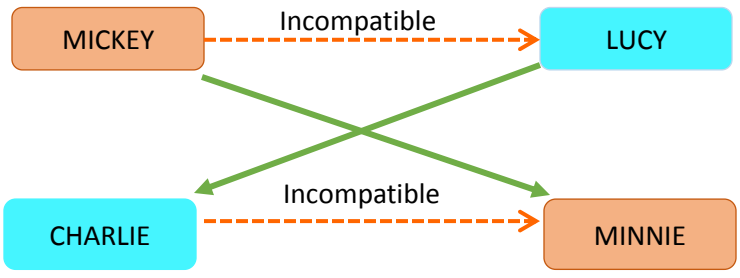
Non-directed donation

In this case, the donor does not have an intended recipient and the match is arranged based on medical compatibility and need. This is also known as an altruistic donor.

Paired exchange donation

This involves two pairs of living kidney donors and transplant candidates who do not have matching blood types. The two candidates "trade" or "swap" donors so that each candidate receives a kidney from a donor with a compatible blood type. For example, in figure 1, Charlie wants to donate to his wife Minnie, but they do not have matching blood types. Mickey wants to donate to his sister Lucy, but they are also not compatible. However these pairs can "swap" donors so that Mickey matches Minnie and Charlie matches Lucy, therefore two transplants are possible. This type of exchange can involve multiple living kidney donor/transplant candidate pairs.

Figure 1



ASSESSMENT AND SELECTION OF LIVING KIDNEY DONORS

There are few studies on living donors to address the appropriate testing required to evaluate a potential candidate or the absolute criteria for allowing an individual to proceed with kidney donation. Some general guidelines, such as the Amsterdam forum on the care of the live kidney donor, have attempted to address the approach to the evaluation and selection of potential living donor candidates. The generally accepted routine screening is detailed in Table 1 and the absolute and relative contraindications are summarized in Table 2. [1,2]

Potential living donor candidates also meet with the independent living donor advocate team. The sole purpose of living donor advocate team is to promote the best interest of, and advocate for the rights of the potential living donor, as well as to assist in obtaining and understanding information regarding kidney donation.

Table 1: Routine screening for potential living kidney donor

History and physical exam	• Detailed medical history including family history of risk factors for kidney disease • Blood pressure and BMI assessment
Laboratory	• Blood group, HLA typing • Complete blood count, prothrombin time, partial thromboplastin time • Comprehensive metabolic panel (electrolytes, transaminase levels, albumin, bilirubin, calcium, phosphorus, alkaline phosphatase) • Infectious diseases serologies: HIV, hepatitis B and C viruses, EBV, CMV, herpes simplex virus, RPR • Fasting glucose, hemoglobin A1c and or OGTT • Lipid panel • Pregnancy test for woman < 50 years old
Urine studies	• Urinalysis for protein, blood and glucose • 24-hour urine creatinine clearance or iodinated/radioactive isotope • Estimation of proteinuria in 24 hour urine collection • Urine culture
Radiographic	• CXR • Spiral CT to evaluate renal anatomy
Cardiopulmonary testing	• Electrocardiogram • Stress test (if indicated) • Echocardiogram (if indicated)
Psychosocial assessment	• Mental health history • Substance abuse history • Detailed assessment of donor's motivation and understanding

Table 2

ABSOLUTE CONTRAINDICATIONS	RELATIVE CONTRAINDICATIONS
▪ Age < 18 years old ▪ Mentally incapable of making informed decision ▪ Uncontrolled hypertension or hypertension with end organ damage ▪ CrCl < 80 mL/min/1.73m2 ▪ Diabetes ▪ Active malignancy or incompletely treated malignancy ▪ Untreated psychiatric conditions ▪ Donor coercion ▪ Nephrolithiasis with high likelihood of recurrence ▪ Persistent infection	▪ CrCl < 2 SD below mean for age ▪ Proteinuria (>150-300mg/24 hours) ▪ Hematuria ▪ Urologic, renal vascular abnormalities or multiple renal vessels ▪ Hypertension ▪ Obesity with BMI 30 - 35 kg/m2 ▪ History of malignancy especially if metastatic ▪ Bleeding disorder ▪ History of thrombosis or embolism ▪ Pre-diabetes or impaired fasting glucose in young donors ▪ Significant cardiovascular disease

SHORT TERM/PERIOPERATIVE RISKS

Most living donor nephrectomies are performed via laparoscopic approach rather than open approach. Similar to other surgeries, the major perioperative risks from donor nephrectomy include bleeding, ileus, pneumothorax, pneumonia, urinary tract infection, deep vein thrombosis with or without pulmonary embolism, wound complications including hernia, and death. Surgical mortality with living kidney donation is very low. One study of over 80,000 living kidney donors between 1994-2009 showed that the 90 day mortality was 3.1 per 10,000 donors. This risk is lower than that of a laparoscopic cholecystectomy (~18 per 10,000 cases) or a non-donor nephrectomy (~260 per 10,000 cases). Older, African American, and hypertensive donors are associated with increased risk for perioperative complications.[3]

Another study based on a national US donor registry from 2008-2012 with administrative records from 98 academic hospitals found that 16.8% donors experienced perioperative complications, most commonly GI (4.4%), bleeding (3%) and respiratory (2.5%). However, only 2.5% donors were affected by major complications. Risk factors for major complications include obesity, pre-donation blood disorders and psychiatric conditions. High volume transplant centers are associated with lower risk.[4]

LONG TERM RENAL RISK

Long term risks are generally rare among healthy individuals who undergo a unilateral nephrectomy. There is an immediate loss of functioning renal mass and GFR during nephrectomy, leading to compensatory hypertrophy in the contralateral kidney, with a 20-40% increase in the GFR of the contralateral kidney. Over time, the hypertrophy of the remaining kidney returns the GFR to ~ 70% of baseline.[5,6] It is important to remember that GFR declines with age, with 4 ml/min/m2 every decade at age <45. This rate of decline increases to 8 ml/min/m2 every decade at age > 45. Lower GFR is associated with increased risk for chronic kidney disease (CKD) and cardiovascular disease, which leads to the concern regarding the long term impact of donor nephrectomy.

Reassuringly, studies on individuals with unilateral nephrectomy showed minimal long term risks. One study looked at World War II servicemen who underwent nephrectomy due to trauma. When they were assessed at 45 years post nephrectomy, these individuals had similar renal function and mortality rates compared to control from the second National Health and Nutrition examination Survey study (NHANES II) study.[7] Many studies in living donors support the findings of unilateral nephrectomy with ESRD risk similar to those of the general population.[8,9]

However, prior studies in living donors primarily used the general population as the comparative group. Results from these studies should be interpreted cautiously as living donors are inherently healthier individuals compared to the general population. Two recent studies with controls selected for baseline good health suggested an increased risk of ESRD attributable to donation. However, the absolute risk remains low. The studies are detailed below:

- A Norway study compared 1901 kidney donors who donated between 1963 and 2007 with 32,621 healthy demographically matched controls from the Health Study of Nord-Trondelag (HUNT) population study. Nine (0.47%) of 1901 donors developed ESRD over a median follow-up time of 15 years compared to 0.07% in non-donors. ESRD among donors were mostly due to immunologic diseases and 85% of donors were biologically related to recipients which raises the question if the higher incidence of ESRD is due to unscreened genetically driven disease process. Mortality between donors and non-donors was similar over the first 15 years but subsequently diverged, with cumulative all-cause mortality at approximately 18% among donors and 13% among non-donors (adjusted HR 1.3, 95% CI 1.1-1.5) at 25 years. Limitations of this study include baseline characteristics with older donors, lack of renal function control group and population not representative of the general population worldwide.[10]

- A U.S. registry study compared 96,217 donors with healthy participants in NHANES III. 99 (0.1%) donors developed ESRD with median follow up of 7.6 years. Estimated lifetime ESRD risk was based on splicing observations for donors observed at different age. The estimated cumulative incidence of ESRD at 15 years was 30.8 per 10,000 donors compared with 3.9 per 10,000 in matched cohort. Sub-group analyses showed higher

incidence of ESRD in older and African-American donors. A major limitation to this study is the repeated use of healthy non-donors in the matching process, which could skew toward underestimation of the risk of ESRD in non-donors.[11]

Although these studies had potential differences between cohorts, the relative increase in risk of ESRD in donors is qualitatively similar. Both studies also suggest that donors with higher pre-donation GFRs will have lower absolute lifetime risks. It is important to remember that despite an increase in relative risk, the absolute risk for ESRD remains low at <1%. Additionally, certain individuals may have a higher lifetime incidence of ESRD such as older individuals, African Americans and those with lower pre-donation GFR. Prospective donors should be informed that their lower residual kidney function after donation may be associated with a higher risk for progression to ESRD if they develop any condition that impacts their renal function.

Impact of ethnicity

African Americans are at higher risk for development of hypertension and CKD compared to the general population. This raises the concern that living kidney donation can increase these risks and recent studies have shown this pattern also occurs after living kidney donation. More recent studies have demonstrated Hispanics have higher incidence of CKD and Diabetes Mellitus compared to Caucasian and are at higher risk for progression to ESRD.[27]

In the previously mentioned US registry study comparing ESRD among 96,217 donors and matched healthy non-donors, African American donors had the highest incidence of ESRD in the 15 years post-donation at 74.7 per 10,000, compared to 32.6 per 10,000 in Hispanic donors and 22.7 per 10,000 in Caucasian donors.[11] In this study, the donation-attributable risk by ethnicity was 50.8, 25.9, and 22.7 ESRD events per 10,000 among African American, Hispanic and Caucasian donors.

Additional studies further addressed the role of ethnicities on renal risk and medical outcome post living kidney donations. These studies are detailed below:

- A study by Lentine et al. used linkage of Organ Procurement and Transplantation Network (OPTN) living donor registry with billing claims from a private health insurer with 6450 living kidney donors, of which 8.2% were Hispanics, 13.1% were African American and 76.3% were Caucasian. At 7.7 years post donation, African American donors had an increased risk of hypertension (adjusted HR(aHR) 1.52; 95% CI 1.23-1.88), diabetes mellitus requiring drug therapy (adjusted HR, 2.31; 95% CI 1.33-3.98) and chronic kidney disease (aHR 2.32; 95% CI 1.48-3.62). These findings were similar in the Hispanic donors post donation. The prevalence of hypertension exceeded estimates in subgroups while prevalence of diabetes did not exceed the general population.[14]

- Another study that analyzed the linked OPTN registry found that at 7 years post donation, a higher portion of African-American compared to Caucasian donors had renal

diagnosis: CKD (12.6 versus 5.6%, aHR 2.32; 95% CI 1.48 – 3.62), proteinuria (5.7% versus 2.6%, aHR 2.27; 95% CI 1.32-3.89), nephrotic syndrome (1.3% versus 0.1%, aHR 15.7; 95% CI 2.97-83), and any renal diagnosis (14.9% versus 9%, aHR 1.71; 95% CI 1.23-2.41).[16]

- A retrospective compared 103 African American donors from 2 transplant centers with 235 matched non-donors from the Coronary Artery Risk Development in Young Adults (CARDIA) prospective cohort study. The frequency of hypertension was higher in donors compared to non-donors (40.8% versus 17.9%, relative risk of 2.4; 95% CI 1.7-3.4) at mean follow up of 6.8 years. This study also had a high number of untreated hypertension among donors, 52.4% of donors diagnosed with hypertension were untreated. [13]

This apparently race-related variation in the risk of post-donation ERSD may, in part, be mediated by the increased incidence of hypertension, diabetes, access to care in these higher risk populations, as well as by unmeasured environmental factors. Recent studies - suggest that renal disease previously attributed to hypertensive nephrosclerosis in African Americans may be genetically mediated by specific polymorphisms in *APOL1* gene. When this was explored in recipients of deceased donor kidneys, it was found that donors with two risk alleles were associated with higher risk of graft loss in the recipients. In a case-control study published from the 1000 Genomes Project, homozygosity for *APOL1* variants was associated with ESRD in African Americans compared with zero risk alleles.[18] The presence of two *APOL1* risk variant alleles has been associated with increased risk of disease processes such as focal segmental glomerulosclerosis, proteinuria, HIV-nephropathy, and more rapid progression of kidney disease among African Americans in the general population. However, it may require a "second hit" leading to decline in kidney function. Further studies are needed to evaluate the impact of *APOL*1 polymorphisms on post-donation and transplant outcomes in African Americans.

African-American potential donors should be counseled regarding higher risks of ESRD and other medical conditions such as hypertension. Some clinical practical guidelines have recommended more stringent selection criteria such as well controlled pre-donation blood pressure. The U.S. registry study demonstrated that Hispanic individuals are at a slightly higher incidence of ESRD compared to Caucasian donors.[11] They were also found to have a higher incidence of hypertension post-donation compared to Caucasian donors from the OPTN linkage study. In addition, the incidence of diabetes is higher in Hispanic individuals compared to Caucasian individuals, which is a risk factor for CKD and ESRD.[35] These donation-attributable risks should be appropriately discussed with all potential donors.

MEDICALLY COMPLEX DONOR

Hypertension

The acceptance of donors with hypertension is variable in the different transplant centers in the U.S. Approximately 41% transplant centers in the U.S. will consider potential donors on one anti-hypertensive medication.

The risk of hypertension may be increased among kidney donors. This risk of increased blood pressure was evaluated in meta-analysis of 48 studies that enrolled 5149 donors (only 6 studies are controlled), which demonstrated that the systolic and diastolic pressures were 6 and 4 mmHg higher in kidney donors.[19] In contrast, a subsequent prospective study of 182 kidney donors demonstrated no difference in blood pressures post donation determined by 24-hour BP monitoring.[28]

Limited studies exist on long-term outcomes of hypertensive donors post donation, and there is even less information regarding African American donors. Most of the studies on outcomes of donors with hypertension are retrospective or prospective observational studies that describe a heterogeneous group of donors that are considered medically complex. All these studies also have different definitions of hypertension (this in part from evolving definition of hypertension) and all excluded donors on 3 or more anti-hypertensive medications. Textor *et al* and Tent *et al* compared donors with hypertension to normotensive donors and found no difference in blood pressure, renal function and urinary protein excretion.[29,30] Lenihan *et al* assessed the effect of hypertension on post-donation BP, renal function and renal volume that demonstrated on difference in post-donation BP, adaptive hyperfiltration and compensatory hypertrophy in 6 months despite glomerulopenia.[21]

These studies suggest that, in the short term, the outcomes for Caucasian donors with pre-existing well-controlled hypertension on less than 2 anti-hypertensive medications will be comparable to donors without hypertension. Further study is needed to quantify the impact of living kidney donation on hypertension risk, and the impact of hypertension on clinical outcomes such as chronic kidney disease and ESRD after donation.

Older

The acceptance of older donors has been controversial as older individuals are more likely to have co-morbidities such as hypertension and lower kidney function. There has been a significant increase in kidney donors from older donors (≥ 60 years old), from 3.6% in 1994 to 9.6% in 2015.[1]

Several studies have demonstrated favorable outcomes of living kidney donation from older donors with the following findings:

- U.S. study of 80,000 living donors to address 90-day mortality post donation found no differences across age groups. However, there was a trend towards higher 12-month mortality in donors ≥ 60 years old compared with young donors (p=0.08). There was a subsequent publication that reported better survival among donors aged 70 or above compared with healthy controls from NHANES III cohort. This finding is likely a reflection of selection bias as donors are typically healthier adults compared to the general population.[3]

- In a study of 3368 older donors (≥55 years) by Reese et al with 8 years follow found no significant difference in all-cause mortality between older donors and healthy demographically matched non-donors from the Health and Retirement Study (4.9 versus 5.6 deaths per 1,000 person-years, HR 0.90, 95% CI 0.71-1.15). There was also no difference in composite outcome of cardiovascular disease (defined as ischemic cardiac disease, congestive heart failure, stroke, peripheral vascular disease) or death (HR 1.02, 95% CI 0.87-1.20).[22]

These studies demonstrate that older age should not exclude individuals from donation. Age is a continuous variable and chronological age does not necessarily match the "physiological age" of a potential donor. There are associations between older donor age and perioperative complications, hypertension, and reduced renal function. It is important to note that older donors demonstrate similar adaptive hyperfiltration and hypertrophy post donation as that seen in younger donors. Therefore, the inferior renal function in older living donors is likely driven by glomerulopenia. Although older donors have higher risk for reduced renal function post-donation, they have fewer years at risk to develop chronic kidney disease, therefore risk factor such as hypertension is less likely to lead to end-stage renal disease when compared to younger donors. Additionally, carefully selected older donors are not at higher risk of death or cardiovascular disease post donation.

Obesity

Obesity is associated with surgical complications and higher risk for hypertension, diabetes mellitus, sleep apnea and cardiovascular disease. Obesity is also associated with proteinuria, chronic kidney disease, and may be associated with ESRD. The Amsterdam report recommended discouraging individuals with BMI >35 kg/m2 from donating, especially when other co-morbidities are present. However, the landscape of living donors with obesity has changed, with 19.5% of living donors with obesity in 2008, up from 14.4% in 2004. This is partially driven by the rise in rate of obesity in the general population.

Obese donors have slightly longer operative times with longer hospitalizations and minor wound complications.[3,4] Laparoscopic nephrectomy has been shown to be safe in selected obese donors and does not result in high rate of major perioperative complications.

A study on the impact of obesity on renal function and proteinuria after solitary nephrectomy for medical reasons showed that obese patients were at higher risk of developing proteinuria,

(90% in obese versus 30% in non-obese) and renal dysfunction (70% in obese versus <10% in non-obese).[23] A meta-analysis showed that most studies following obese donors were heterogeneous with short follow up and those with longer follow up had conflicting results on changes in GFR. Two more recent studies showed that obese donors are not at higher risk for reduced renal function, one with mean follow up of 11 years and the other 7 years. However obese donors are at higher risk for hypertension, cardiovascular disease and also microalbuminuria.[24]

BMI > 35 kg/m2 is considered a contraindication in most transplant centers. It is important to consider factors such as muscle mass and, body habitus when assessing the BMI. Overweight and obese donors are counseled to lose weight and the potential risks, including perioperative, operative and long-term medical consequences, are carefully discussed.

PREGNANCY AFTER DONATION

Pregnancy in healthy women is associated with significant alterations in systemic hemodynamics. There is a decrease in systemic vascular resistance and mean arterial pressure despite a 40-50% increase in cardiac output and an increase in plasma volume. At the level of the kidney, there are striking changes with an increase in glomerular filtration rate (GFR), renal plasma flow and a small increase in kidney size with dilatation of the collecting system. The presence of vasodilatory hormones, increase in renal plasma flow and decrease in oncotic pressure are thought to be responsible for the increase in GFR during pregnancy. Given these changes to renal physiology during pregnancy, it is important to consider the impact of kidney donation on maternal and fetal outcomes.[31]

The incidence of hypertensive disorders of pregnancy in healthy non-donors is about 10%. The weighted average incidence of gestational hypertension is 7.9%, pre-eclampsia 3.3% and eclampsia is 0.06%. In the United States, premature birth and low birth weight have an overall incidence of 2% to 13%.[32,33]

Evidence of pregnancy risks among living donors is mostly derived from observational studies. The early studies were small, single center experiences that demonstrated no increased risk for maternal or fetal complications. However in 2009, two retrospective cohort studies challenged those findings, as they showed higher rates of gestational hypertension and preeclampsia.

- The first, used registry data from Norway to identify 326 donors among whom 726 pregnancies were reported, 106 of which were post donation in 69 donors. After adjustment for maternal age, birth order and year of birth, the incidence of preeclampsia was higher in donors than that among the general population (5.7% vs 3.1%). The mean maternal age among donors was 5 years older than among non-donors and that comparison did not account for such between-group differences. Although there is a higher incidence of preeclampsia in donors, the overall event rates were low and there were no differences in rates of low birth weight or pre-term birth.[34]

- The second study reported on 1085 living donors at University of Minnesota, among whom a total of 3123 pregnancies were reported; 490 pregnancies occurred after donation in 239 donors. Overall event rates of pregnancy complications were comparable to those in general population. However, the incidence of fetal loss, gestation hypertension and preeclampsia were higher among women who had pregnancies after donation. The study outcomes were obtained via donor recall in a survey.[22]

An important consideration in interpretation of the results in these two studies is that the risk of complications in pregnancy increases with maternal age and some of these women became pregnant for the first time after kidney donation. Additionally, these studies did not use controls matched in age and other characteristics, and no information was provided on blood pressure values or the accuracy of antihypertensive treatments used (one of the study relied entirely on self-reported survey data).

In 2015, a retrospective cohort study assessed the risk of gestational hypertension or preeclampsia and maternal and fetal outcomes in living kidney donors.[26] It compared 85 donors (131 pregnancies) with 510 healthy matched non-donors (788 pregnancies) with comparable risk factors for gestational hypertension or preeclampsia. The median follow up was 11 years and maximum at 20 years. The incidence of gestational hypertension or preeclampsia was higher in donors compared to non-donors (11% vs 5%, OR (odds ratio) for donors 2.4, 95% CI 1.2-5.0). There was no significant increase in risk of other adverse pregnancy outcomes such as caesarean section post-partum hemorrhage, rates of pre-term birth or low birth weight. A sub-group analysis showed that the OR for developing preeclampsia or gestational hypertension was greater in individuals older than 32 years old at time of pregnancy.

Although there is an increased risk for gestational hypertension or preeclampsia in donors compared to the non-donors, the overall event rates remain low and most of these individuals had uncomplicated pregnancies after donation. All donor candidates of childbearing age should be informed and counseled about these risks. Pregnancy post-donation should be considered "higher risk" with rigorous surveillance for hypertension and preeclampsia.

Further research is needed on pregnancy outcomes among donors including assessment for additional risk among donor subgroups such as impact of obesity and ethnicities (African Americans and Hispanic have higher baseline rates of preeclampsia).

FOLLOW UP AND MANAGEMENT OF PRIOR KIDNEY DONORS

In an ideal world, all prior kidney donors should have lifelong follow up for medical surveillance. Unfortunately, this is rare. Geographic distances from transplant centers and cost issues significantly impact the likelihood of donor follow up. Current United Network for Organ Sharing (UNOS) guidelines require transplant programs to report information about living

donors post-donation at post-operative discharge, 6 months, 12 months and 24 months. Currently post-donation follow-up is variable among transplant centers. Although donors are counseled to follow up with primary care physicians, many remains lost to follow up. Financial reason is one of the factor that impact follow up and it raises the question if donors should receive lifetime insurance to provide access to healthcare post donation.

The focus of follow up should be to minimize additional risk factors for development of CKD and ESRD. Donors are counseled to follow up with their primary care physicians at least annually. In addition to assessment of renal function and proteinuria, they should also be evaluated for development of other disease process that may increase risk for CKD and ESRD such as hypertension and diabetes mellitus. Table 3 provides a general guideline on the management of any prior kidney donors.

Table 3: General guideline for management of prior kidney donors

ANNUAL PRIMARY CARE VISIT
1) Assessment of the following: ▪ **Blood pressure** ▪ **Kidney function, with serum creatinine** ▪ **Urinalysis to assess for albuminuria and proteinuria** ▪ **Blood glucose** ▪ **BMI** **2) Management of hypertension in those with HTN pre-donation and those who develop HTN post-donation.** **3) Review of medication list for nephrotoxic agents. Counsel patient on avoidance of NSAIDs use.** **4) Tobacco cessation for the smokers** **5) Evaluation for diabetes and appropriate management for those who develop diabetes.** **6) Weight loss for the obese donors** ▪ **Consider referral to obesity specialist and bariatric surgery for individuals who are morbidly obese and unable to achieve weight loss.** **7) Early referral to nephrology for individuals who develop chronic kidney disease (CKD) or proteinuria.**

CONCLUSIONS

Since the first successful living kidney donation in 1954, more studies have improved our understanding of the short term and long-term risks of donation. Though more recent studies suggest that ESRD risk attributable to donation is higher than previously reported, it is important to remember that the absolute risk is still very low. Further studies are needed to evaluate long-term outcomes for donors with pre-existing co-morbidities, and lifetime risks in young (<30 years) donors. Efforts are to be made to address the need for a donor registry and also to establish long-term follow up for prior donors.

REFERENCE

1. Organ procurement and transplant network (OPTN)/United Network for Organ Sharing (UNOS). National data reports, transplants by donor type and latest data.
2. Delmonico F; Council of the Transplantation Society; A report of the Amsterdam Forum on the Care of the Live Kidney Donor Data and medical guidelines. Transplantation 79 [Suppl]; S53-S66,2005.
3. Segev DL, Muzaale AD, Caffo BS, et al. Perioperative mortality and long term survival following live kidney donation. JAMA 2010; 303:959
4. Lentine KL, Lam NN, Axelrod D, et al. Perioperative complications after living kidney donation: A national study. Am J Transplant 2016; 16:1846.
5. Pabico RC, McKenna BA, Freeman RB. Renal function before and after unilateral nephrectomy in renal donors. Kidney Int 1975; 8:166.
6. Kasiske BL, MA JZ, Louis TA, et al. Long-term effects of reduced renal mass in humans. Kidney Int. 1995; 48:814.
7. Narkun-Burgess DM, Nolan CR, Norman JE, et al. Forty-five year follow up after uninephrectomy. Kidney Int 1993; 43:1110.
8. Lam NN, Lentine KL, Levey AS, et al. Long-term medical risks to the living kidney donor. Nat Rev Nephrol 2015; 11:411.
9. Ibrahim HN, Foley R, Tan L, et al. Long-term consequence of kidney donation. N Engl J Med 2009; 360:459.
10. Mjoen G, Hallan S, Hartmann A, et al. Long-term risks for kidney donors. Kidney Int 2014; 86:162.
11. Muzaale AD, Massie AB, Wang MC, et al. Risk of end stage renal disease following live kidney donation. JAMA 2014; 311:579.
12. Lam NN, Lentine KL, Garg AX. End-stage renal disease risk in live kidney donors:what have we learned from two recent studies? Curr Opin Nephrol Hypertens 2014; 23:592.
13. Doshi MD, Goggins MO, Li L, et al. Medical outcomes in African American live kidney donors: a matched cohort study. Am J Transplant 2013; 13:111.
14. Lentine KL, Schnitzler MA, Xiao H, et al. Racial variation in medical outcomes among living kidney donors. N Engl J Med 2010; 363:724.
15. Nogueira JM, Weir MR, Jacobs S, et al. A study of renal outcomes in African American living kidney donors. Transplantation 2009; 88:1371.

16. Lentine KL, Schnitzler MA, Garg AX, et al. Race, relationship and renal diagnosis after living kidney donation. Transplantation 2015; 99:1723.
17. Cohen DM, Mittalhenkle A, Scott DL, et al. African American living-kidney donors should be screened for APOL1 risk alleles. Transplantation 2011; 92:722.
18. Reeves-Daniel AM, DePalma JA, Bleyer AJ, et al. The APOL1 gene and allograft survival after kidney transplantation. Am J Transplant 2011;11:1025.
19. Boudville N, Prasad GB, Knoll G, et al. Meta-analysis: risk for hypertension in living kidney donors. Ann Intern Med 2006; 145:185.
20. Garg AX, Prasad GV, Thiessen-Philbrook HR, et al. Cardiovascular disease and hypertension risk in living kidney donors: an analysis of health administrative data in Ontario, Canada. Transplantation 2008; 86:399.
21. Lenihan CR, Busque S, Derby S, et al.The association of predonation hypertension with glomerular function and number in older living kidney donors. J Am Soc Nephrol 2015; 26:1261.
22. Reese PP, Bloom RD, Feldman HI, et al. Mortality and cardiovascular disease among older live kidney donors. Am J Transplant 2014; 14:1853.
23. Praga M, Hernadez E, Herrero JC, et al. Influence of obesity on the appearance of proteinuria and renal insufficiency after unilateral nephrectomy. Kidney Int 2000; 58:2111.
24. Noguiera JM, Weir MR, Jacobs S, et al. A study of renal outcomes in obese living kidney donors. Transplantation 2010; 90:993.
25. Ibrahim HN, Akkina SK, Leister E, et al. Pregnancy outcomes after kidney donation. Am J Transplant 2009; 9:825.
26. Garg AX, Nevis IF, McArthur E, et al. Gestational hypertension and pre-eclampsia in living kidney donors. N Engl J Med 2015; 372:124.
27. Lora CM, Daviglus M, Kusek, JW, et al. Chronic kidney disease in United States Hispanic: a growing public health problem. Ethn Dis 2009; 19:466.
28. Kasiske BL, Anderson-Haag T, Israni AK, et al. A prospective controlled study of living kidney donors: three-year follow up. Am J Kidney Dis. 2015;66:114.
29. Textor SC, Taler SJ, Driscoll N, et al. Blood pressure and renal function after kidney donation from hypertensive living donors. Transplantation 2004;78:276.
30. Tent H, Sanders JS, Rook M, et al. Effects of preexistent hypertension on blood pressure and residual renal function after donor nephrectomy. Transplantation 2012; 93:412.
31. Baylis C and Davison JM. Renal physiology in normal pregnancy. In:Floege J, Johnson RJ, Feehaly J eds. *Comprehensive clinical nephrology*. 4th ed. 2010 Edinburgh:Mosby.
32. Hsieh HL, Lee KS, Khoshnood B, et al. Fetal death rate in the United States, 1979-1990:Trend and racial disparity. Obstet Gynecol 1997; 89:33.
33. Hawkins JL, Bimbach DJ. Maternal mortality in the United States: Where are we going and how will we get there? Anesth Analg 2001; 93:1.
34. Reisaeter AV, Roislien J, Henriksen T, et al. Pregnancy and birth after kidney donation: the Norwegian experience. Am J Transplant 2009;9:820.
35. Schneiderman N, Llabre M, Cowie CC, et al. Prevalence of diabetes among Hispanics/Latinos from Diverse backgrounds: The Hispanic Community Health Study/Study of Latinos (HCHS/SOL). Diabetes Care 2014;37:2233.