

**ASSOCIATION BETWEEN HISTOLOGICAL ABNORMALITIES IN TIME-  
ZERO RENAL BIOPSIES AND  
POST-DONATION ESTIMATED GLOMERULAR FILTRATION RATE  
IN LIVE DONORS**

by

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## I. Abstract

**Background:** Time-zero renal biopsies (T0-RBx) of living donor kidneys may reveal histological abnormalities at the time of organ recovery. The association between T0-RBx and long-term post-donation kidney function in living donors remains unclear.

**Methods:** We abstracted the extent of glomerulosclerosis, interstitial fibrosis, mesangial matrix increase, arteriolar hyalinosis, and intimal thickening from T0-RBx of 253 living donors at our institution. We then constructed a binary composite score, moderate/severe abnormality (MSA), from the factors abstracted and linked it to donor estimated glomerular filtration rate (eGFR) obtained from post-donation medical records with median (interquartile range) follow-up time of 7.1 (4.2 – 9.2) years. We used multilevel mixed-effects linear regression to model the association between MSA and eGFR trajectory over time.

**Results:** 22.9% of donors had one or more MSAs. In an unadjusted model, there was no evidence of difference in post-donation eGFR between MSA and no MSA donors (difference in eGFR  $-3.17_{0.76}$  mL/min/1.73m<sup>2</sup>,  $p = 0.1$ ). The association was further attenuated after adjusting for donor age at transplant, sex, and race (difference in eGFR  $-0.04_{3.64}$  mL/min/1.73m<sup>2</sup>,  $p = 0.99$ ).

**Conclusions:** There is no evidence of association between minor histological abnormalities at time of organ donation and post-donation eGFR in living donors.

Among donors cleared to donate, biopsy results do not predict post-donation renal health.

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## 1. Introduction

The kidney is a vital organ in the human body. Among its many functions, it helps the body discard toxic wastes.<sup>1</sup> Clinically healthy individuals sometimes choose to donate a kidney to patients with faulty kidneys. It is important to investigate how such donations impact the renal function of these living donors.

### *Chronic kidney disease, end-stage renal disease, and therapies*

Chronic Kidney Disease (CKD) is a condition in which the kidneys' function starts to deteriorate over a time period greater than 3 months.<sup>2</sup> Many health complications may arise due to this gradual loss of kidney function.<sup>3</sup> Based on a patient's glomerular filtration rate (GFR) and albuminuria, which are measures of renal function, he/she is categorized into one of the five stages of CKD (Figure 1).<sup>2</sup> Stage 5 CKD, also known as end-stage renal disease (ESRD), indicates renal failure. Once a patient reaches ESRD, renal replacement therapy is needed.<sup>4</sup>

				Persistent albuminuria categories Description and range		
				A1	A2	A3
				Normal to mildly increased	Moderately increased	Severely increased
				<30 mg/g <3 mg/mmol	30-300 mg/g 3-30 mg/mmol	>300 mg/g >30 mg/mmol
GFR categories (ml/min/1.73 m <sup>2</sup> ) Description and range	G1	Normal or high	≥90			
	G2	Mildly decreased	60-89			
	G3a	Mildly to moderately decreased	45-59			
	G3b	Moderately to severely decreased	30-44			
	G4	Severely decreased	15-29			
	G5	Kidney failure	<15			

Green: low risk (if no other markers of kidney disease, no CKD); Yellow: moderately increased risk; Orange: high risk; Red, very high risk.

**Figure 1.** Prognosis of CKD by GFR and albuminuria categories. G1-G5 represent the five stages of CKD.<sup>2</sup>

The two major types of renal replacement therapy are dialysis and kidney transplantation.<sup>5</sup> In the United States (US), there were 114,813 newly reported cases in 2012. On December 1<sup>st</sup>, 2012, there were 636,905 prevalent cases of ESRD.<sup>5</sup> From the newly reported cases, 108,129 were on dialysis and 2,803 received a kidney transplant. From the prevalent cases, 443,119 were on dialysis and 175,978 had a functioning graft.<sup>5</sup>

***Living kidney donation***

There are two types of donors for kidney transplantation: deceased and living. In the US, 5,617 out of 17,305 kidney transplants performed in 2012 came from living donors.<sup>5</sup>

Living donor kidney transplants have several advantages to the kidney recipient, including a relatively shorter time to transplant and better graft function.<sup>5</sup> However, there is no benefit to the donor and the long-term risk of undergoing a living donor nephrectomy remains unclear.

In order to qualify for kidney donation, a living donor must be a consenting adult who is generally in good health and have normal kidney function.<sup>6</sup> Individuals who have some form of kidney disease, diabetes, hypertension, cancer, heart disease, hepatitis, infectious disease, psychiatric problems, kidney stones, obese, or are ongoing drug abusers are usually ineligible for donation.<sup>6</sup> Despite these clinical guidelines that are in place to ensure a healthy pool of donors, renal biopsies of the donated kidney reveal histological abnormalities at time of donation (time-zero renal biopsies, T0-RBx).<sup>7-10</sup>

### ***Renal histological abnormalities***

The four major morphological components of the kidney that can be affected by disease are: glomeruli, tubules, interstitium, and vasculature.<sup>11</sup> The glomeruli respond to chronic injury mainly through basement membrane thickening; hyalinosis (deposition of hyalin, an extracellular amorphous material composed of plasma proteins, in the glomerular blood vessels); and glomerulosclerosis (deposition of an extracellular collagenous matrix).<sup>11</sup> Moreover, abnormalities in the mesangium, a meshwork of cells and extracellular matrix that support glomeruli tufts, are also an indicator of renal pathogenesis.<sup>11</sup> Thus, the presence of these histological abnormalities may suggest chronic renal injury.<sup>11</sup>

Other indicators of renal abnormalities involve the tubules, interstitium, and vasculature. Progressive glomerular injury is usually followed by chronic injuries to the other components of the kidney, such as the tubules and the interstitium, commonly causing tubulointerstitial fibrosis (tubular damage and interstitial inflammation).<sup>11</sup> Injury to the renal vasculature typically results in muscle cell proliferation, extracellular matrix deposition, and in turn, intimal thickening.<sup>11</sup>

Studies have reported sporadic correlations between renal histological abnormalities and pre-donation clinical living donor characteristics.<sup>7,12,13</sup> However, donor age and blood pressure were reported to be independently associated with renal histological abnormalities.<sup>12,13</sup>

Several studies have investigated the association of histological abnormalities in the donated kidney and post-transplant renal graft function in kidney recipients. For deceased donor kidneys, there appears to be a consensus that histological abnormalities impact post-transplant graft function, and are reported to be a better predictor of graft survival in comparison to donor clinical characteristics.<sup>14-16,19</sup> For living donor kidneys, a study by Ma *et al.* analyzing 72 living donor kidneys reported that histological abnormalities did impact post-transplant graft function.<sup>17</sup> However, a study by Lee *et al.*, investigating 146 living donor kidney transplant recipients, found no evidence of association between minor subclinical histological abnormalities detected in T0-RBx and post-transplant graft function.<sup>18</sup> Both studies performed a retrospective analysis of data collected at their institution.

A few studies have investigated the association of renal histological abnormalities in the donated kidney and short-term post-donation function of the sister

kidney in the living donors. These studies have reported that minor renal histological abnormalities at time of organ donation did not impact short-term post-donation estimated glomerular filtration rate (eGFR) in living donors (a maximum mean follow-up time of 3.5 years).<sup>12,13</sup> However, the impact of histological abnormalities on long-term post-donation eGFR remains unclear. Moreover, these studies have looked at post-donation eGFR at particular time points and not eGFR trajectories over time. Therefore, a study looking at long-term post-donation eGFR trajectories over time is much needed.

### ***Measuring renal function***

A common measure of renal function is eGFR. Creatinine in the patient's blood, a muscle metabolic waste product, obtained through tests such as a comprehensive metabolic panel (CMP), basic metabolic panel (BMP), or renal function panel, is used in eGFR calculations.<sup>20</sup> There are different equations used to calculate eGFR using a combination of serum creatinine and other patient characteristics.<sup>21-24</sup> eGFR calculations assume a stable creatinine level and therefore, might not be suitable for certain groups of people such as pregnant women, patients with acute illness, obese patients, and/or patients with extremes of muscle mass.<sup>21</sup>

### ***Objective***

The objective of this study is to investigate the association between histological abnormalities in T0-RBx and post-donation eGFR in living kidney donors.

### ***Public health significance***

Evidence of association between histological abnormalities in T0-RBx and changes in post-donation renal function in living donors would inform treatment decisions for current living donors and future potential donors, especially when renal biopsies are thought of as a safe diagnostic tool.<sup>25,26</sup> First, for those living donors who already donated a kidney, T0-RBx results may inform post-transplant preventative care. Second, for future potential living donors, a pre-donation biopsy may inform the decision to donate. Conversely, a *lack* of association between T0-RBx abnormalities and post-donation renal function would reassure donors who had such abnormalities, and inform future donors and healthcare providers that mild pre-donation histological abnormalities need not be a contraindication for transplantation.

## 2. Methods

### *Study Design*

We adopted a retrospective cohort study design. Upon Institutional Review Board approval, we attempted to contact participants over the phone or through mail to survey them about their donation, and obtain consent to abstract their medical records. We used information reported in the T0-RBx, reported in their medical records, to obtain our exposure of interest and details about the biopsies and laboratory techniques used. Information regarding our outcome of interest was also extracted from these medical records.

### *Study population*

Our source population consisted of 1,678 individuals who underwent living donor nephrectomy at the Johns Hopkins Hospital (JHH) between August 1970 and October 2014. 847 of these individuals consented to medical record abstraction. Our inclusion criterion was living kidney donors who had a T0-RBx. 297 out of 847 had a T0-RBx, between February 1997 and June 2012. We excluded T0-RBx with fewer than 10 glomeruli ( $n = 44$ ), since ascertainment of histological abnormalities may not be reliable in these biopsies.

### *T0-RBx histological evaluation*

Surgical pathologists at JHH evaluated the T0-RBx for histological abnormalities within a short time after biopsy collection (typically one pathologist per biopsy). The types of biopsies performed were either needle (commonly) or wedge biopsies. Light

microscopy was used to analyze all samples using the following stains: hematoxylin and eosin, periodic acid-Schiff (PAS), Mallory trichrome, and Jones' silver methenamine.

### ***Exposure of interest***

Since these were time-zero biopsies, the identification and scoring of histological abnormalities overlapped with the Banff criteria.<sup>27-29</sup> Five variables were abstracted from the surgical pathology laboratory reports of the T0-RBx: glomerulosclerosis (GS), interstitial fibrosis (IF), mesangial matrix increase (MI), arteriolar hyalinosis (AH), and intimal thickening (IT).

GS was quantified as the percentage of observed glomeruli that were globally sclerotic. IF was assessed as a visual estimate of the percentage of cortical area that had IF and categorized as: IF in  $\leq 5\%$  of cortical area (minimal), 6-25% (mild), 26-50% (moderate), or  $> 50\%$  (severe). MI was quantified as the presence (moderate/severe) or absence of MI.

AH was categorized into four groups: No PAS-positive hyaline thickening, mild-to-moderate PAS-positive hyaline thickening in at least one arteriole, moderate-to-severe PAS-positive hyaline thickening in more than one arteriole, or severe PAS-positive hyaline thickening in many arterioles. IT was also categorized into four groups: no chronic vascular changes, vascular narrowing of up to 25% of luminal area by fibrointimal thickening of arteries (mild), increased severity of changes with 26-50% narrowing of vascular luminal area (moderate), or severe vascular changes with  $> 50\%$  narrowing of vascular luminal area (severe). If the pathology report did not mention the presence of vasculature, we assumed that there were none observed in the sample.

We then constructed a binary composite score, moderate/severe abnormality (MSA). A biopsy was considered to have MSA if it had at least one moderate/severe abnormality in any of: IF, MI, AH, IT, or  $GS \geq 15\%$ .

### ***Post-donation eGFR***

We obtained post-donation serum creatinine from the patient medical records. We used the CKD-EPI creatinine equation to calculate eGFR using the donor's serum creatinine level obtained from the medical records, age at measurement, sex, and race.<sup>22</sup>

### ***Statistical analysis***

For continuous variables, the median and interquartile range (IQR) were reported. For categorical variables, the percentage was reported. We compared our study population to kidney living donors at the JHH who did not have a T0-RBx. Within our study population, we looked at donor characteristics stratified by MSA status. Unpaired *t*-tests and Fisher exact tests were used to make statistical comparisons.

We used scatterplots and non-parametric lowess to visualize eGFR trajectories over time, stratified by exposure of interest. We then used multilevel mixed-effects linear (MMEL) regression to perform longitudinal data analysis. A variety of MMEL regression models were constructed, including models with spline terms for time, allowing for random intercepts, and/or allowing for random slopes. Based on the AIC values and likelihood ratio tests, the optimal model was selected. The selected model was then used to model the unadjusted and adjusted relationship between the exposure

of interest and eGFR over time. Adjusted models were controlled for donor age at donation, sex, and race.

Statistical significance was established at a  $p$ -value less than 0.05. All analyses were performed using STATA 13.0 for Mac (College Station, TX). Confidence intervals are reported as per the Louis and Zeger method.<sup>30</sup>

### 3. Results

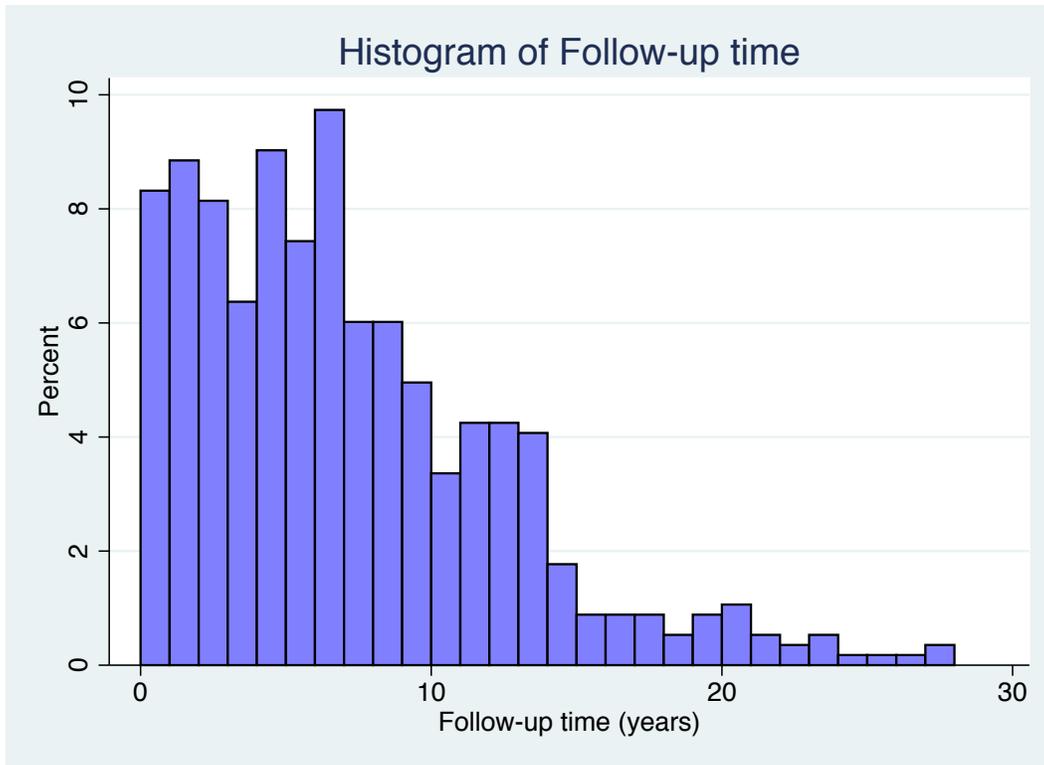
#### *Study population*

Our study population did not differ much from the general living donor pool at JHH. There was no difference between donors who had a T0-RBx and those who did not with regards to race ( $p = 0.3$ ), gender ( $p = 0.8$ ), post-donation follow-up time ( $p = 0.6$ ), and mean post-donation eGFR per donor ( $p = 0.7$ ) (Table 1). Age was marginally statistically significant ( $p = 0.046$ ); biopsied donors being slightly older [median (IQR) age is 46.9 (39.4 – 54.1) years for biopsied, and 45.5 (36.5 – 53.4) years for not biopsied]. The number of post-donation eGFR measurements per donor was higher in biopsied donors (3) as compared to non-biopsied donors (1) ( $p < 0.001$ ). The majority of our study participants were white and female (90.2% and 64.3%, respectively). The overall median (IQR) follow up time was 7.1 (4.2 – 9.2) years and the median (IQR) mean post-donation eGFR per donor was 62.0 (52.7 – 71.0) mL/min/1.73m<sup>2</sup> (Figure 2).

Characteristics	Biopsied (N=253)	Not Biopsied (N=550)	p-value
Age, years <i>median (IQR)</i>	46.9 (39.4 - 54.1)	45.5 (36.5 – 53.4)	<b>0.046</b>
Race, %			
White	90.2%	84.7%	0.3
Black	6.7%	11.1%	
Others	3.1%	4.2%	
Gender, %			
Female	64.3%	63.6%	0.8
Male	35.7%	36.4%	
Follow-up time, years <i>median (IQR)</i>	7.1 (4.2 – 9.2)	5.3 (2.3 – 11.8)	0.6
Mean post-donation eGFR per person, mL/min/1.73m <sup>2</sup> <i>median (IQR)</i>	62.0 (52.7 – 71.0)	62.3 (54.3 – 71.8)	0.7
Number of post-donation eGFR measurements per donor <i>median (IQR)</i>	3	1	<0.001

Notes: Bolded p-value statistically significant at  $\alpha = 0.05$ .

**Table 1.** Living kidney donor characteristics stratified by time-zero biopsy availability.



**Figure 2.** Distribution of post-donation follow-up time.

Donors with MSA were older than donors with no MSA at time of organ donation. The median (IQR) age for MSA donors was 52.7 (46.2 – 57.6) years, and the median (IQR) age for no MSA donors was 46.5 (38.5 – 53.1) years ( $p < 0.001$ ). Race, gender, post-donation follow-up time, mean post-donation eGFR per donor, and number of post-donation eGFR measurements per donor did not differ by MSA status (Table 2).

<b>Characteristics</b>	<b>MSA (N=47)</b>	<b>No MSA (N=158)</b>	<b>p-value</b>
Age, years <i>median (IQR)</i>	52.7 (46.2 – 57.6)	46.4 (38.5 – 53.1)	<b>&lt;0.001</b>
Race, %			
White	93.6%	92.4%	0.5
Black	6.4%	5.1%	
Others	0.0%	2.5%	
Gender, %			
Female	61.7%	66.5%	0.5
Male	38.3%	33.5%	
Follow-up time, years <i>median (IQR)</i>	6.7 (4.3 – 8.7)	7.7 (4.7 – 9.4)	0.4
Mean post-donation eGFR per donor, mL/min/1.73m <sup>2</sup> <i>median (IQR)</i>	60.0 (51.8 – 73.0)	62.6 (55.0 – 72.0)	0.1
Number of post-donation eGFR measurements per donor <i>median (IQR)</i>	3	4	0.8

Notes: Bolded p-value statistically significant at  $\alpha = 0.05$ .

**Table 2.** Living kidney donor characteristics stratified by exposure of interest, moderate/severe histological abnormality (MSA) in time-zero biopsies.

### ***Exposure of interest***

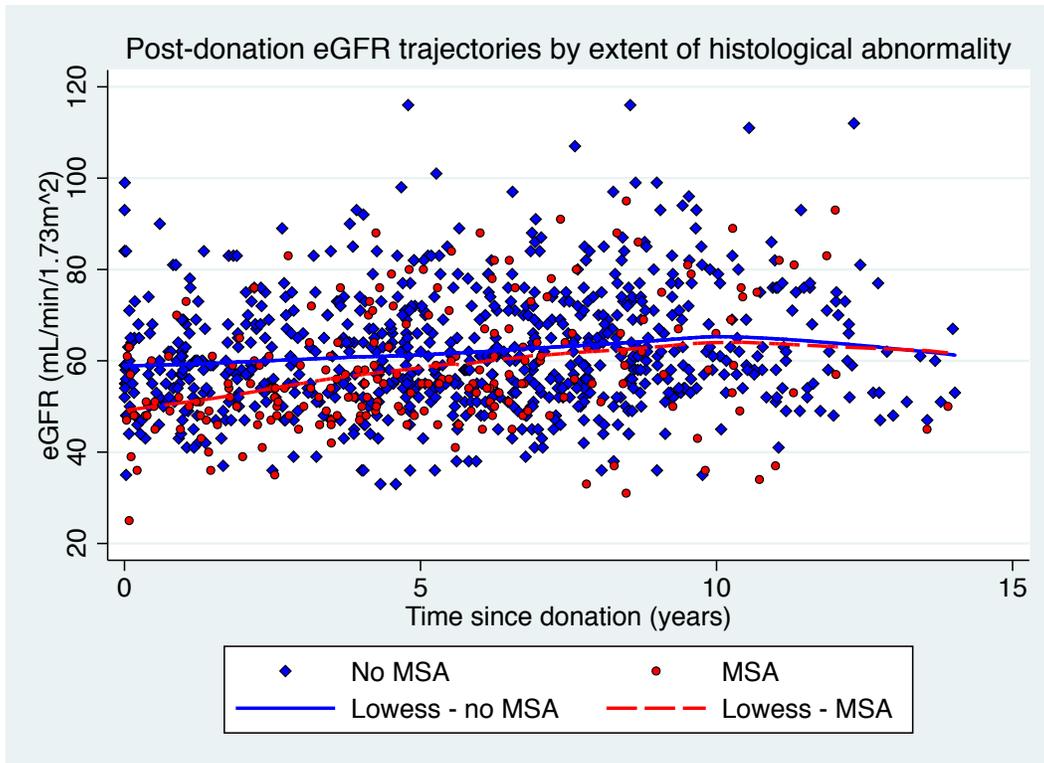
The majority of living donors had no or minor histological abnormalities indicated by their T0-RBx. However, a significant percentage of living donors had MSA, 22.9%. Specifically, the majority of the donors had GS < 15% (85.5%), minimal IF (73.0%), no MI (95.3%), no HA (64.0%), and no IT (68.0%) (Table 3). 77% of MSA donors scored moderate/severe in only one category and 23% of MSA donors scored moderate/severe in two or more categories.

<b>Histological Abnormalities</b>	
Glomerulosclerosis (GS)	
< 15%	85.5%
≥ 15%	14.5%
Interstitial fibrosis (IF)	
Minimal	73.0%
Mild	25.4%
Moderate	1.6%
Severe	0%
Mesangial increase (MI)	
No MI	95.3%
Increase	4.7%
Hyalinosis (HA)	
No HA	64.0%
Mild	35.1%
Moderate	0.4%
Severe	0.4%
Intimal thickening (IT)	
No IT	68.0%
Mild	29.4%
Moderate	2.2%
Severe	0.4%
Moderate/severe abnormalities (MSA)	
No MSA	77.1%
MSA	22.9%

**Table 3.** Histological abnormalities detected via time-zero biopsies.

### *Statistical analysis*

A scatterplot of post-donation eGFR stratified by MSA status indicated that initial post-donation eGFR was lower for MSA donors compared to no MSA donors. However, this difference appeared to attenuate over time. For both MSA and no MSA donors, post-donation eGFR trajectory appeared to gradually increase over time until 10 years, after which the trajectory appeared to decrease slightly (Figure 3).



**Figure 3.** Post-donation eGFR trajectories stratified by moderate/severe abnormalities (MSA) detected via time-zero biopsies.

Based on the AIC values, we selected MMEL models that allowed for random intercepts and slopes, with no spline term for time at 10 years. In an unadjusted MMEL, at any given time point, MSA did not appear to be associated with post-donation eGFR – a difference of  $-3.17$   $_{-0.76}^{0.76}$  mL/min/1.73m<sup>2</sup> between MSA versus no MSA ( $p = 0.1$ ). This association was attenuated and remained statistically insignificant after adjusting for donor age, sex, and race ( $-3.57$   $_{-0.04}^{3.64}$  mL/min/1.73m<sup>2</sup>,  $p = 0.99$ ) (Table 4). There was no evidence of interaction between MSA and time following donation ( $p = 0.5$ ).

	Change in eGFR (mL/min/1.73m <sup>2</sup> )	
	Unadjusted model	Adjusted model <sup>A</sup>
Per year	0.54 <b>0.81</b> 1.08	0.49 <b>0.76</b> 1.02
MSA (vs no MSA)	-7.10 -3.17 0.76	-3.57 <b>0.04</b> 3.64
Age (per 10y)	-	-7.03 <b>-5.55</b> -4.06
Sex (vs Male)	-	-2.51 <b>0.60</b> 3.70
Race (vs White)	-	
Black		-0.74 <b>5.77</b> 12.27
Others		-13.07 <b>-2.15</b> 8.77

Notes: Bolded p-value statistically significant at  $\alpha = 0.05$ .

<sup>A</sup>Model adjusted for donor age, sex and race.

**Table 4.** Multilevel mixed-effects linear regression models of post-donation eGFR over time.

#### 4. Discussion

The majority of our study population did not have moderate/severe renal abnormalities at time of organ donation. Among those who did have moderate/severe renal abnormalities, the majority scored moderate/severe in only one of the five categories. Our results indicate that after adjusting for donor age at donation, sex, and race, there is no association between those moderate/severe histological abnormalities and post-donation eGFR over time in living kidney donors.

These results are consistent with previous findings that studied short-term post-donation eGFR.<sup>11,12</sup> A retrospective study by Chauhan *et al.* reported that eGFR was similar in donors with and without moderate/severe changes in T0-RBx (mean follow-up time of 3.5 years).<sup>11</sup> In addition, a prospective study by Choi *et al.* reported that 1-year post-donation eGFR (n = 121) was not affected by histological abnormalities at T0-RBx.<sup>12</sup>

There are a few limitations to our study. One limitation is small sample size; not all living donors at JHH had a T0-RBx. The majority of the biopsied donors were done so for research purposes on incompatible kidney transplantations (which do not bias our

results). Another limitation is potential ascertainment bias in post-donation eGFR. eGFR values were obtained from the medical records. If this was indeed a bias in our results, then it would likely be in the non-null direction, assuming that less healthy donors were seeking healthcare more often than healthy donors. Despite this potential bias, our results are null.

The strengths of our study include relatively longer post-donation follow-up time compared to previous studies. Our median post-donation follow-up was about 7 years, whereas other studies reported a maximum mean follow-up time of 3.5 years. Another strength of our study is that we investigated post-donation eGFR *over time*, not at a specific post-donation time point.

It must be noted that the findings of this study cannot be generalized to the general population. This study population consisted of clinically healthy individuals with relatively minor renal histological abnormalities. Therefore, it would be inappropriate to make inferences about the association between renal histological abnormalities and renal function in the general population based on these study findings.

Although our study had a relatively longer post-donation follow-up time than previous studies, we cannot make inferences beyond 7 years. Therefore, future studies are needed to investigate the association between histological abnormalities at time-zero and post-donation eGFR over a longer follow-up period, and using a larger sample size. Moreover, it will be useful to investigate each category separately (e.g.: the association between IF and post-donation eGFR) rather than a composite exposure, to aid in the understanding of the underlying biology.

In conclusion, there was no evidence of an association between histological abnormalities detected at time of organ donation and post-donation eGFR in living kidney donors. Future studies are needed to confirm these findings. However, these findings serve to reassure living donors, at least in the short-term. Moreover, among donors clinically cleared for donation, there is no evidence suggesting that T0-RBx further informs donor selection.

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## VIII. Curriculum vitae

### **PART I: General Information**

**Name:** Lara M. Fahmy

**Home Address:** 501 Saint Paul Street, Apartment #1104, Baltimore, Maryland 21202

#### **Contact Information:**

Telephone (216) 513-0760

E-mail [lfahmy1@jhu.edu](mailto:lfahmy1@jhu.edu)

**Born:** July 8<sup>th</sup>, 1992, Omaha, Nebraska

**Citizenship:** U.S. Citizen

**Languages:** Bilingual English/Arabic  
Good in French

#### **Education:**

**2013–present Johns Hopkins University**, Baltimore, Maryland

**Master of Science (Sc.M.)**

Bloomberg School of Public Health

Department of Epidemiology

Grade Point Average: 4.00 on a 4.00 Scale

**2009–2013 Case Western Reserve University**, Cleveland, Ohio

**Bachelors of Science in Engineering (B.S.E.)**

Case School of Engineering

*Major:* Biomedical Engineering; *Concentration:* Tissue Engineering

*Minor:* Chemistry

Grade Point Average: Overall 3.85, Math & Science 3.94 both on a 4.00 Scale

**2008–2009 University of London**

**General Certificate of Education (G.C.E.)**

Advanced Levels in Biology and Chemistry

Overall Grade: A

Rank in Class: 1<sup>st</sup> of 66 Students

**2007–2008 University of London**

**General Certificate of Secondary Education (G.C.S.E.)**

Ordinary Levels in Biology, Chemistry, Physics, Mathematics, Information and Communication Technology, Religious Studies, English Language, English Literature, Arabic, and French

Overall Grade: A\* (Distinction)

Rank in Class: 1<sup>st</sup> of 243 Students

**Certification:**

2013–present Maryland State certified HIV Tester and Counselor

**Computer Programming Skills:**

Excellent Matlab, PSPICE, and LabView programming skills.

Very good Stata programming skills.

**Memberships in Organizations and Professional Societies:**

2015–present Trainee Member, American Society of Transplant Surgeons

2013–present Student Member, General Epidemiology and Methodology Journal Club, Johns Hopkins Bloomberg School of Public Health

2013–present Student Member, Johns Hopkins Graduate Muslim Student Association, Johns Hopkins University

2009–2013 Student Member, Biomedical Engineering Society, Case Western Reserve University

2009–2013 Student Member, Muslim Student Association, Case Western Reserve University

**Honors and Awards:**

2015 Anna Huffstutler Stiles Scholarship, Department-Awarded Scholarship, Department of Epidemiology, Johns Hopkins Bloomberg School of Public Health

2014 Miriam E. Brailey Fund Award, Department-Awarded Scholarship, Department of Epidemiology, Johns Hopkins Bloomberg School of Public Health

2013 *Magna Cum Laude*, Commencement Honors, Case Western Reserve University

2013 Community Service Medal, Mortar Board, National College Senior Honor Society, Case Western Reserve University

2012 Best Prototype Design, for Paraplegic Soccer Ball Kicking, EBME 370, Principles of Biomedical Engineering Design, Case Western Reserve University

2012 Tau Beta Pi, The Engineering Honor Society, Case School of Engineering, Case Western Reserve University

2012 Alpha Eta Mu Beta, The National Biomedical Engineering Honor Society, Case School of Engineering, Case Western Reserve University

2012 Mortar Board, The National College Senior Honor Society, Case Western Reserve University

2010 The National Society of Collegiate Scholars, Case Western Reserve University

2010 The Golden Key International Honor Society, Case Western Reserve University

2009–2013 Case Dean's High Honors List, Case School of Engineering, Case Western Reserve University

2005–2009 Academic Merit Scholarship, for Outstanding Academic Achievement, Saint Mary's Catholic High School, Dubai, United Arab Emirates

2005–2008 Prefect, Saint Mary's Catholic High School, Dubai, United Arab Emirates

## **Volunteer Activities:**

- 2013–2014 Heartland Obstetrics and Gynecology, Omaha, Nebraska**  
**Volunteer Medical Assistant**  
Take patients medical histories and prepare patients for physician. Assist physician with patients' examinations and minor procedures. Prepare patients samples for laboratory work. Call-in patients' medication. Organize patients' charts and paperwork. Manage the front desk, clinic phone, and patient/surgery scheduling.
- 2012–2013 Cleveland School of Arts, Cleveland, Ohio**  
**Volunteer Peer Tutor**  
Tutor high school art students who need help with pre-calculus and pre-algebra.
- 2012–2013 Church of the Covenant, Cleveland, Ohio**  
**Volunteer Peer Tutor**  
Tutor high school students in the local community who need help with mathematics and/or science.
- 2011–2012 University Hospitals, Rainbow Babies and Children's Hospital, Cleveland, Ohio**  
**Child Life Activities Volunteer**  
Provide activities for pediatric patients' whose age range from newly born to 18 years of age. Decorate the activity room. Play with children in the activity room or by patient bedside. Feed and entertain babies.
- 2010–2011 Heartland Obstetrics and Gynecology, Omaha, Nebraska**  
**Student Observer**  
Shadow and observe physicians in clinic and operating room. Got a chance to observe normal deliveries, and scrub in on caesarean sections and laparoscopic procedures.
- 2007–2009 Saint Mary's Catholic High School, Dubai, United Arab Emirates**  
**Community Service Volunteer**  
Participated in my high school's community service programs, which included: assisting nurses in mobile clinics by giving out band-aids, and hot and cold packs to patients; and assisting counselors in designing leaflets for various community counseling programs.

## **Leadership Experience:**

- 2014–present Student Mentor, Department of Epidemiology, Johns Hopkins Bloomberg School of Public Health
- 2014–present Master's Representative Chair, Department of Epidemiology, Johns Hopkins Bloomberg School of Public Health
- 2012–2013 Team Leader, Senior Capstone Design Team, Department of Biomedical Engineering, Case Western Reserve University
- 2012–2013 Middle Eastern Representative, Interfaith Board, Case Western Reserve University
- 2011–2013 Middle Eastern Representative, Diversity and Inclusion, Undergraduate Student Government, Case Western Reserve University
- 2010–2013 Secretary for the 2011-2012 academic year, Member since 2010, Middle Eastern Cultural Association, Case Western Reserve University

## **PART II: Research and Teaching Contributions**

### **RESEARCH EXPERIENCE**

**2014–present Johns Hopkins University School of Medicine, Baltimore, Maryland**  
**Department of Surgery,**  
**Professor Dorry L. Segev Laboratory,**  
**Graduate Student Researcher**

**Association between Histological Abnormalities in the Kidney and Post-donation eGFR in Live Donors.** Mild histological abnormalities reported at the time of kidney donation may be associated with post-donation renal function in live donors. My thesis focus is investigating this association.

**2014–present Johns Hopkins University School of Medicine, Baltimore, Maryland**  
**Department of Gynecology and Obstetrics**  
**Clinical Fellow Laura Londra,**  
**Data Analyst**

**Ovarian reserve and the availability of at least one euploid embryo after preimplantation genetic screening.** I designed and performed the data analysis to investigate the relationship between the level of ovarian reserve in women and the odds of obtaining at least one euploid embryo in women undergoing IVF. After adjusting for the woman's age, the odds of obtaining at least one euploid embryo is higher for women with high ovarian reserve as compared to women with low ovarian reserve. A manuscript describing this work is currently in preparation for publication.

**2013–2014 Johns Hopkins University, Baltimore, Maryland**  
**Center for AIDS Research (CFAR),**  
**Generation Tomorrow,**  
**Research Assistant**

Generation tomorrow is a training and hands-on field experience program for students and community-based health workers in Baltimore. The program is designed to increase awareness, detection, and prevention of HIV and Hepatitis C infections. It also aims to create cultural-competency among health professionals. As research assistant I HIV test/counsel individuals in large scale HIV testing events such as “National Black HIV/AIDS Awareness Day” hosted by Sisters Together and Reaching (STAR), a community-based organization. Attend HIV/AIDS conferences and symposia hosted by CFAR such as “Bridging the Gap Symposium.” Within CFAR I was particularly involved with the following study:

**AIDS Linked to the IntraVenous Experience (ALIVE) Study.** I HIV test and counsel past/current injection drug using participants in a community based research clinic. Assist participants with Audio Computer-assisted Self-interviewing (ACASI). Performed functional assessments on participants. Shadow and assist nurse practitioners with participants' examinations. Assist clinic staff with administrative work such as mailing, data entry, sorting, and filing.

**2010–2013 Case Western Reserve University, School of Medicine, Cleveland, Ohio  
Wolstein Research Center,  
Department of Experimental Pathology,  
Professor Xiongwei Zhu Laboratory,  
Student Researcher**

**An Analysis of Post-Mortem Interval on Immunohistochemistry.** I looked at the RNA content of brain tissue frozen at different time intervals, post-mortem. I used gel and real-time PCR techniques to analyze the degradation pattern of RNA in the tissue, specifically looking at  $\beta_2$  microglobulin (B2M) and glyceraldehyde 3-phosphate dehydrogenase (GAPDH) expression. I find that if the tissue stays unfrozen for more than twenty-four hours (post-mortem), significant RNA degradation takes place. A manuscript describing this work is currently in preparation for publication.

**Alzheimer's Disease (AD) and Mislocalization of Cyclin-Dependent Kinase 11 (CDK11).** CDK11 is required for sister chromatid cohesion during completion of mitosis, it is usually only expressed in cells undergoing mitosis, during the G<sub>2</sub>/M phase of the cell cycle. Terminally differentiated post-mitotic neurons do not typically express CDK11. I find increased cytoplasmic CDK11 expression in AD, which is in an Amyloid Precursor Protein (APP) dependent fashion. This indicates that CDK11 may signal cell cycle re-entry in AD neurons, presenting a novel function for APP. This work has been published in *Cellular and Molecular Biology Letters*.

## TEACHING EXPERIENCE

### **Teaching Assistant, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD**

*Spring 2015 TAed the following courses:*

*PH.140.623 Statistical Methods in Public Health III*

*PH.340.753 Epidemiologic Methods III*

Lead laboratory discussions. Hold office hours. Grade student homework, quizzes, and exams. Pilot exams, labs, and assignments.

### **Teaching Assistant, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD**

*Fall 2014 PH.140.622 Statistical Methods in Public Health II*

Hold weekly office hours. Grade student homework, quizzes, and exams.

### **Peer Tutor, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD**

*Fall 2014 Tutored the following courses:*

*PH.140.621 Statistical Methods in Public Health I*

*PH.140.622 Statistical Methods in Public Health II*

### **Administrative Teaching Assistant, Case School of Engineering, Case Western Reserve University, Cleveland, Ohio**

*Spring 2013 ENGR 131 Introduction to Computer Programming (Matlab Programming)*

Run weekly review and homework help sessions. Grade student exams. Edit Matlab code pertaining to class work. Create surveys and PowerPoint slides to facilitate student learning. Answer student emails pertaining to administrative issues. Administer make-up quizzes. Supervise the work of the other teaching assistants to ensure the course runs smoothly.

### **Teaching Assistant, Case School of Engineering, Case Western Reserve University, Cleveland, Ohio**

*Spring 2013 EBME 310/360 Principles of Biomedical Instrumentations*

Grade student quizzes, labs, and exams. Write questions and rubrics for exam and homework questions. Meet with students one-on-one to provide assistance when necessary. Run weekly laboratory sessions when needed.

*Fall 2012 ENGR 131 Introduction to Computer Programming (Matlab Programming)*

Run weekly laboratory sessions. Grade student quizzes, labs, and exams. Meet with students one-on-one to provide assistance when necessary.

### **Peer Tutor, Educational Services for Students, Case Western Reserve University, Cleveland, Ohio**

*2012-2013 Tutored the following courses:*

*EBME 308, Biomedical Signals and Systems*

*EBME 306, Introduction to Biomedical Materials*

*ARAB 102, Beginning Arabic II*

### **Peer Tutor, Saint Mary's Catholic High School, Dubai, United Arab Emirates**

*2007-2009 Tutored Biology, Chemistry, Physics, Mathematics, French, and English.*

## PART III: Bibliography

### Publications:

1. **Fahmy, L. M.**, Massie, A. B., Orandi, B. J., Bagnasco, S. M., Alejo, J. L., Boyarsky, B. J., Anjum, S. K., Montgomery, R. A., Dagher, N. N., & Segev, D. L. (2015) Association between histological abnormalities in time-zero renal biopsies and post-donation eGFR in live donors. (in preparation).
2. Londra, L. C., **Fahmy, L. M.**, & Kaufmann, R. (2015) Euploid embryo after preimplantation genetic screening. (in preparation).
3. **Fahmy, L. M.**, Blair, J. A., Siedlak, S. L., Rodgers, M., Castellani, R., Smith, M. A., Lee, H. G., & Zhu, X. (2015) An analysis of post-mortem interval on immunohistochemistry. (in preparation).
4. Londra, L., Tobler, K., **Fahmy, L.**, Kaufmann, R., Ross, R., & Hearn, W. G. (2014) Ovarian reserve and the availability of at least one euploid embryo after preimplantation genetic screening. *Fertil. Steril.* **102**, e152.
5. Bajić, V. P., Su, B., Lee, H. G., Kudo, W., Siedlak, S. L., Zivković, L., Spremo-Potparević, B., Djelic, N., Milicevic, Z., Singh, A. K., **Fahmy, L. M.**, Wang, X., Smith, M. A., & Zhu, X. (2011) Mislocalization of CDK11/PITSLRE, a regulator of the G<sub>2</sub>/M phase of the cell cycle, in Alzheimer disease. *Cell. Mol. Biol. Lett.* **16**, 359-372.
6. **Fahmy, L. M.** (2012) Blinding Light. Photography, *Case Reserve Review*. [http://cdn.casereservereview.org/pdfs/CRR\\_fall12.pdf](http://cdn.casereservereview.org/pdfs/CRR_fall12.pdf)
7. **Fahmy, L. M.** (2008) The Unexpected. Write Time, *Gulf News*. <http://gulfnews.com/about-gulf-news/al-nisr-portfolio/notes/articles/write-time-1.92614>

### Oral Presentations:

1. **Fahmy, L. M.**, Massie, A. B., Orandi, B. J., Bagnasco, S. M., Alejo, J. L., Boyarsky, B. J., Anjum, S. K., Montgomery, R. A., Dagher, N. N., & Segev, D. L. *Association between Histological Abnormalities in Time-Zero Renal Biopsies and Postdonation eGFR in Live Donors*. Oral Presentation at: American Transplant Congress 2015, Philadelphia, Pennsylvania, May 3<sup>rd</sup>, 2015.

### Poster Presentations:

1. **Fahmy, L. M.**, Massie, A. B., Orandi, B. J., Bagnasco, S. M., Alejo, J. L., Boyarsky, B. J., Anjum, S. K., Montgomery, R. A., Dagher, N. N., & Segev, D. L. *Postdonation eGFR in Live Donors and Histological Abnormalities in Time-Zero Renal Biopsies*. Poster presented at: The 2015 Department of Surgery Research Poster Session, Department of Surgery, Johns Hopkins University School of Medicine, February 26<sup>th</sup>, 2015, Baltimore, Maryland.
2. **Fahmy, L. M.**, Massie, A. B., Orandi, B. J., Bagnasco, S. M., Alejo, J. L., Boyarsky, B. J., Anjum, S. K., Montgomery, R. A., Dagher, N. N., & Segev, D. L. *Association between Histological Abnormalities in Time-Zero Renal Biopsies and Postdonation eGFR in Live Donors*. Poster presented at: The Delta Omega Poster Session, Johns Hopkins Bloomberg School of Public Health, February 3<sup>rd</sup>-6<sup>th</sup>, 2015, Baltimore, Maryland.