

## Supplementary Appendix

This appendix has been provided by the authors to give readers additional information about their work.

Supplement to: Ibrahim HN, Foley R, Tan L, et al. Long-term consequences of kidney donation. *N Engl J Med* 2009;360:459-69.

## **APPENDIX:**

### Measurement of GFR and Urinary Protein

GFR was measured using the plasma disappearance of iohexol (1). Via a small polyethylene catheter placed in an antecubital vein, we injected 5 mL of iohexol solution (647 mg of iohexol; 300 mg of iodine per mL). From the contralateral arm, via a second antecubital vein catheter, we then obtained serial samples at 120, 150, 180, 210, and 240 minutes ( $\pm 15$  sec). Plasma was stored at  $-20^{\circ}\text{C}$  for HPLC determination of iohexol concentration. To analyze the plasma profile, we used a 1-compartment model system with all data fitted by a nonlinear regression iterative program. We chose the plasma disappearance of iohexol method because it does not require timed urine collections, which may result in incomplete bladder emptying and lead to significant variability in the GFR measurement, and in view of its excellent correlation with inulin clearance; the gold standard of measuring GFR. The coefficient of variation (CV) of the iohexol GFR method at our center is consistently  $< 10\%$  (2).

To compare our results with previous reports that used serum creatinine alone or used it to estimate GFR, and recognizing that large differences exist in serum creatinine assays across laboratories (3), we sent 25 samples for creatinine measurement (range 0.6 to 2.3 mg/dL) to the Cleveland Clinic Core Biochemistry Laboratory. This range was chosen since it would encompass the range observed in the overwhelming majority of donors, as we have shown in our previous studies (2,4-5). The aforementioned laboratory is where serum creatinine was assayed for the Modification of Diet in Renal Disease (MDRD) study using the Beckmann Rate Jaffe<sup>2</sup>/ CXR Synchron method, which is based on the kinetic alkaline picrate reaction (3). We compared the Cleveland Clinic's results

with ours from the University of Minnesota laboratories which use an identical method and instrument. The results from the both institutions were virtually identical. The Pearson correlation coefficient between the measurements at the 2 institutions was 0.9965. Moreover, the mean difference between the measurements was 0.0125 mg/dL with a standard deviation of 0.03 mg/dL. From the calibrated creatinine, we calculated the MDRD GFR.

Urinary albumin excretion rate was measured on a first-void urine sample on the day of the GFR measurement by nephelometry (6). The CV of this measurement at our laboratory is 5%. Urinary albumin excretion is expressed as the urinary albumin/creatinine ratio (ACR). We defined normoalbuminuria as ACR < 17 mg/g creatinine for men and < 25 mg/g for women; microalbuminuria, ACR 17 to 250 mg/g creatinine for men and 25 to 355 for women; macroalbuminuria, ACR > 250 mg/g creatinine for men and > 355 mg/g for women (7).

#### Quality of Life Assessment

The SF-12v2 contains fewer items than the SF-36, but is designed to provide comparable measures of health status in eight core domains: physical functioning, physical role functioning, bodily pain, general health perceptions, vitality, social functioning, emotional role functioning and mental health (8,9). Physical (PCS) and Mental (MCS) Component Summary scores are formed by combining these domain scores. PCS and MCS scores from the SF-36 and SF-12v2 have been extensively tested and shown to be valid, responsive and reliable across a wide range of clinical and healthy populations. SF-12 and SF-36 were administered at the time of iohexol GFR measurement.

### Appendix for Table 3

A total of 1445 donor nephrectomies have been performed at the University of Minnesota more than 20 years ago; 1035 donors have responded to our surveys over the years. Seven hundred sixty-eight have provided serum creatinine results which allowed us to estimate GFR; 904 provided height, weight, systolic and diastolic blood pressure; 391 provided the results of a lipid panel and glucose; 1035 responded to our questions regarding the self-reported conditions of diabetes, cancer, coronary heart disease, use of anti-hypertensive drugs and current smoking status. No information is available regarding the urinary albumin-to-creatinine ratio.

### References for the Appendix

1. Gaspari F, Perico N, Ruggenti P, et al. Plasma clearance of nonradioactive iohexol as a measure of glomerular filtration rate. *J Am Soc Nephrol* 1995;6(2):257-263.
2. Ibrahim HN, Rogers T, Tello A, Matas A. The performance of three serum creatinine-based formulas in estimating GFR in former kidney donors. *Am J Transplantation* 2006;6:1479-1485.
3. Stevens L, Coresh J, Greene T, Levey A. Assessing kidney function: Measured and estimated glomerular filtration rate. *N Engl J Med* 2006;354:2473-2483.
4. Najarian JS, Chavers BM, McHugh LE, Matas AJ. 20 years or more of follow up of living kidney donors. *Lancet* 1992;340(8823):807-810.
5. Ramcharan T, Matas A. Long term (20-37 years) follow-up of living kidney donors. *Am J Transplant* 2002;2(10):959-964.
6. Chavers BM, Simonson J, Michael AF: A solid phase fluorescent immunoassay for the measurement of human urinary albumin. *Kidney Int* 1984;25:576-578.
7. Levey AS, Coresh J, Balk E, et al. National Kidney Foundation practice guidelines for chronic kidney disease: Evaluation, classification, and

stratification. *Ann Intern Med* 2003;139:137-147.

8. Ware JE Jr., Kosinski M, Turner-Bowker DM, Gandek B. How to Score Version 2 of the SF-12® Health Survey (With a Supplement Documenting Version 1). Lincoln, RI: QualityMetric, 2002.
9. Ware JE, Kosinski M, Keller SD. SF-36 Physical and Mental Health Summary Scales: A User's Manual. Boston, MA: Health Assessment Lab, 1994.