ONLINE SUPPLEMENT

FATTY KIDNEY, HYPERTENSION, AND CHRONIC KIDNEY DISEASE: THE FRAMINGHAM HEART STUDY

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Short Title: Fatty kidney, hypertension and CKD

Supplemental Tables and Figures

Table S1. Imputed blood pressure and renal function outcomes as functions of log-transformed renal sinus fat. Increments in outcome per standard deviation increase in log-transformed renal sinus fat (standard errors shown in parentheses) are presented for continuous outcomes. Odds ratios (95% confidence interval) for a standard deviation increase in log-transformed renal sinus fat are presented for dichotomous outcomes.

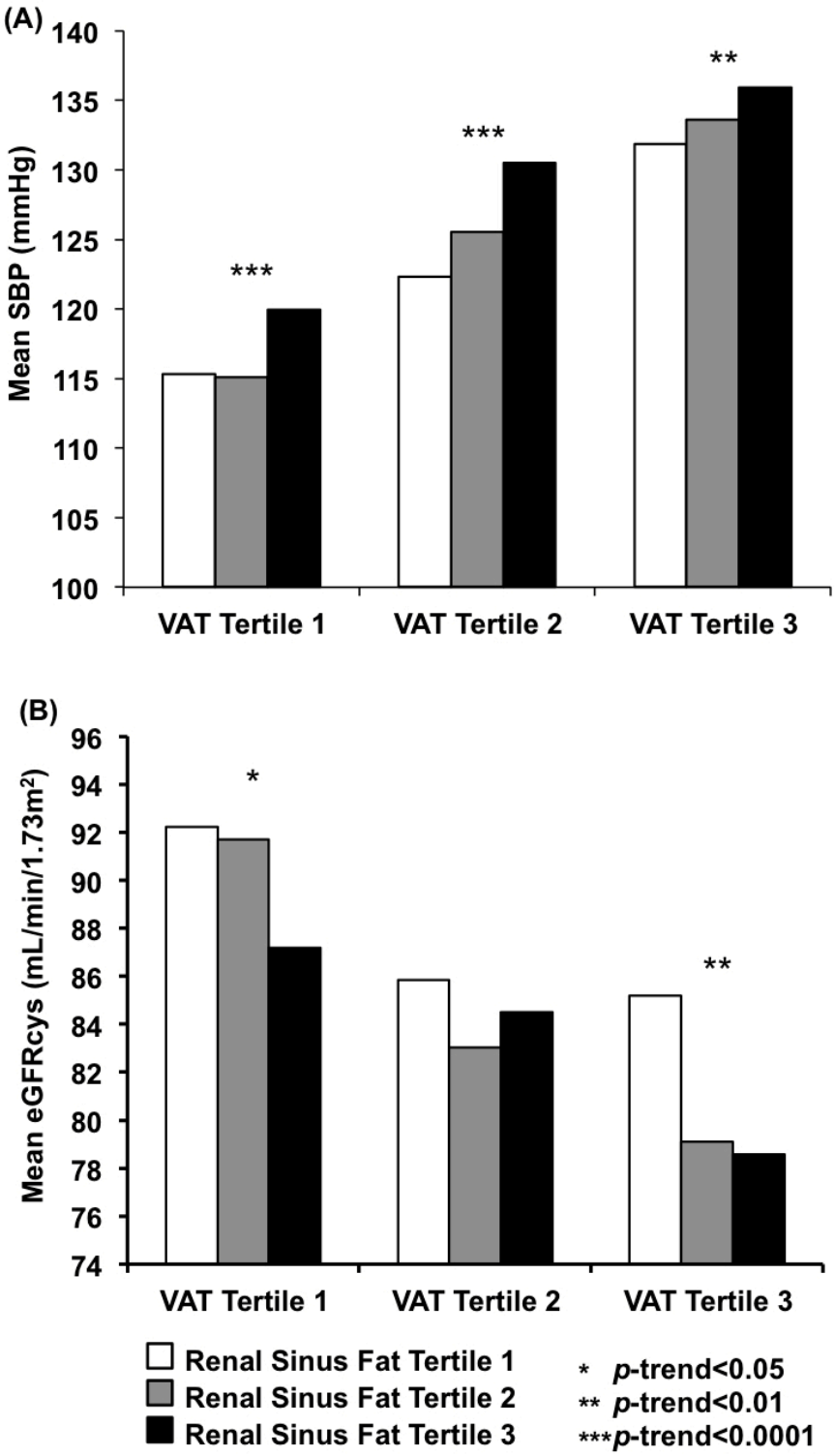
Model outcome of interest	Age and sex	Multivariable†	Multivariable + BMI	Multivariable + VAT
Continuous outcomes				
Systolic blood pressure (mmHg)	2.8 (0.3) p<0.0001	2.7 (0.3) p<0.0001	1.2 (0.3) p=0.0005	0.7 (0.4) p=0.045
Diastolic blood pressure (mmHg)	1.6 (0.2) p<0.0001	1.5 (0.2) p<0.0001	0.7 (0.2) p=0.0007	0.6 (0.2) p=0.005
$eGFR_{cys}$ ($mL/min/1.73m^2$)	-1.82 (0.52) p=0.0004	-1.13 (0.52) p=0.03	-0.0005 (0.54) p=0.99	-0.15 (0.58) p=0.80
$eGFR_{crea}$ ($mL/min/1.73m^2$)	0.70 (0.33) p=0.03	0.59 (0.34) p=0.08	0.33 (0.35) p=0.36	0.14 (0.38) p=0.71
Dichotomous outcomes				
Hypertension	1.59 (1.43 – 1.76) p<0.0001	1.57 (1.42 – 1.75) p<0.0001	1.26 (1.12 – 1.41) p<0.0001	1.11 (0.99 – 1.26) p=0.08
CKD_{cys}	2.33 (1.48 – 3.67) p=0.0003	2.07 (1.30 – 3.28) p=0.002	1.67 (1.04 – 2.67) p=0.03	1.69 (1.01 – 2.81) p=0.045
CKD_{crea}	1.04 (0.82 – 1.32) p=0.75	0.85 (0.66 – 1.08) p=0.19	0.82 (0.63 – 1.07) p=0.14	0.81 (0.62 – 1.08) p=0.15

Abbreviations: BMI=body mass index; $eGFR_{crea}$=estimated glomerular filtration rate using the modified MDRD study equation; $eGFR_{cys}$=estimated glomerular filtration rate using the cystatin-C only CKD-EPI equation; VAT=abdominal visceral adipose tissue volume; CKD_{crea}=chronic kidney disease status based on $eGFR_{crea}$; CKD_{cys}=chronic kidney disease status based on $eGFR_{cys}$.

*Sex-specific cut points for fatty kidney: ≥0.71 cm^2 in men; ≥0.445 cm^2 in women.

†Multivariable models are adjusted for age and sex as well as covariates listed below by outcome: $eGFR_{cys}$, $eGFR_{crea}$, CKD_{cys}, CKD_{crea}: diabetes status, current hypertension medication use, systolic blood pressure, current smoking status, high-density lipoprotein cholesterol level. Imputed systolic blood pressure, diastolic blood pressure, hypertension: Current smoking status, high alcohol intake, physical activity index.

Figure S1.



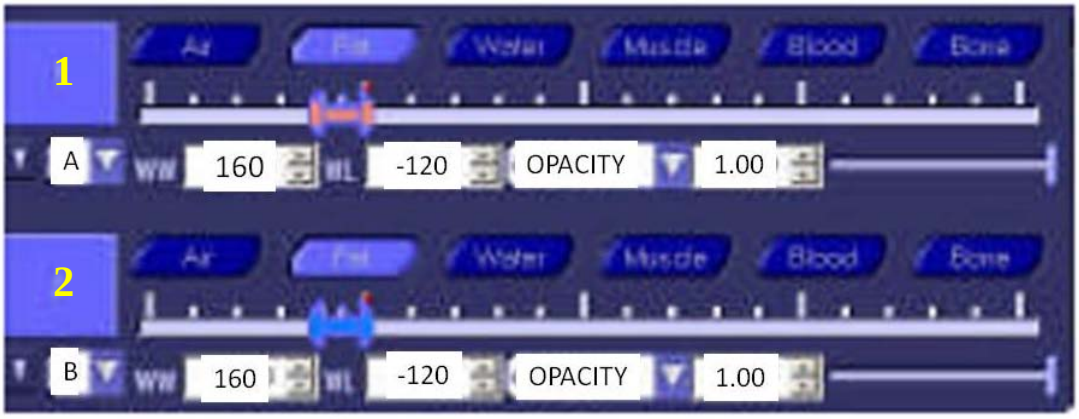
S1. (A) Mean imputed systolic blood pressure (SBP) and (B) mean cystatin-C-based estimated glomerular filtration rate ($eGFR_{cys}$) across tertiles of renal sinus fat within tertiles of abdominal visceral adipose tissue (VAT).

Supplemental Methods

Framingham Heart Study Renal Sinus Fat Measurement Protocol

1) Before performing the first renal sinus fat measurement during a session, open the Aquarius 3D Workstation software and confirm that the Fat template has the correct settings. This can be checked by opening the 3D Setting and confirming that the settings in A and B match the settings in **Protocol Figure 1** below (WW = 160, WL = -120, Opacity = 1.00).

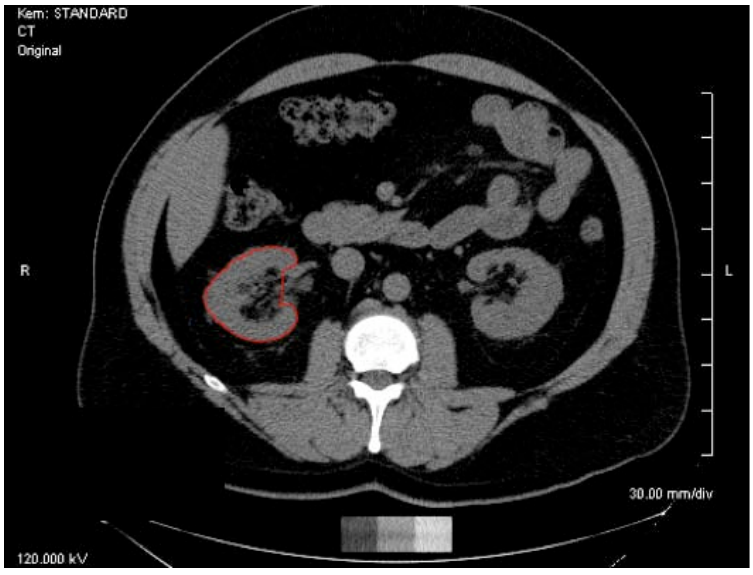
Protocol Figure 1: Aquarius 3D Workstation W/L, Opacity, and Color Settings for the renal sinus fat measurement protocol.



2) Select scan from the patient name column.
3) Select 30-slice option from the box at the lower left of the screen.
4) Use the 30-slice scout to identify the renal sinus in the right kidney, based on the following steps:
    i. **Identify the end slice:** Find first slice in which the opening of the renal sinus is visualized record slice number (slice *n*). Select slice *n*+1 as the end slice. For example, if slice 10 is the first slice in which the renal sinus opening is visualized, then select slice 11 as the end slice.
    ii. **Identify the start slice:** Find last slice in which the opening of the renal sinus is visualized and record slice number (slice *m*). Select slice *m*-1 as the start slice. For example, if slice 3 is the last slice in which the renal sinus opening is visualized, then select slice 2 as the end slice. If the opening of the renal sinus is visualized in slice 1, then select slice 1 as the start slice.
5) Click on **3D** tab at the top of the screen.
6) Select the **template** tab and use the mouse to double-click on the **FAT 3** icon.
7) On **mask** tab, select **curve.**
8) On **mask** tab, select **axial.**
9) Respond "**yes**" to "Do you want to reset the current mask?"
10) **Final slice selection and renal sinus fat measurements**

a. Of the range of selected slices (slice numbers *n* through *m)* in the renal sinus, identify the slice/slices of 'maximum fat' based on visual inspection. These slices should appear similar visually, with the renal sinus containing the largest amount of black coloring on the CT scan.
b. If an odd number of slices are identified in step 10a, then select the middle slice within the range of selected slices for the measurement. If an even number of slices are identified in 10a, then identify the two middle slices within the range of selected slices and choose from these two slices the slice that anatomically superior for the measurement.
    i. If only one slice is identified in step 10a, then select this slice for the renal sinus fat measurement.
c. Scroll to the slice selected in step 10b for the measurement and use the mouse cursor while holding down the mouse left-click button to trace around edge of the kidney. Make sure that the tracing is just within the boundary of the kidney such that surrounding visceral fat is not accidentally captured in the measurement.
d. The opening of the renal sinus will be present in the CT scan. Use a straight line to trace across the opening of the renal sinus. The boundary between inside and outside the renal sinus used for measurements should be based on anatomical characteristics where a dimple forms at the edge of the renal sinus opening (See **Figure 2** below for an example of tracing across the renal sinus).
e. Only trace the kidney on the one slice selected for measurement.
f. Once the kidney has been traced, use right-click button on mouse to keep the traced area; the green line traced around the kidney will turn red after using the right-click button (**Protocol Figure 2**).

Protocol Figure 2: Abdominal CT scan with a manual tracing of the right kidney in red.

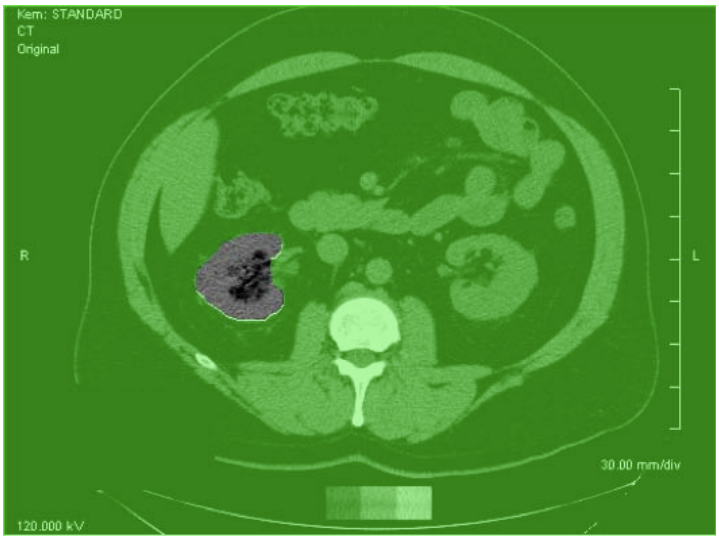


11) Check the tracing surrounding the right kidney in the measurement slice. If a mistake in the tracing is identified, then the measurement must be performed again, starting from Step 2 in the protocol.
12) Once the tracing of the right kidney slice is completed, select **Keep Region**. The red outlined region (**Protocol Figure 2**) will now be shaded green (**Protocol Figure 3**).

Protocol Figure 3: Abdominal CT scan with the selected region based on the manual tracing of the right kidney highlighted in green after selecting **Keep Region** in step 12.

13) Drag icon in **Box A** to **Box B** and click "**Reverse.**" The green shading on the CT scan will now be reversed, as shown in **Protocol Figure 4**.

Protocol Figure 4: Abdominal CT scan with the selected region based on the manual tracing of the right kidney highlighted in green.

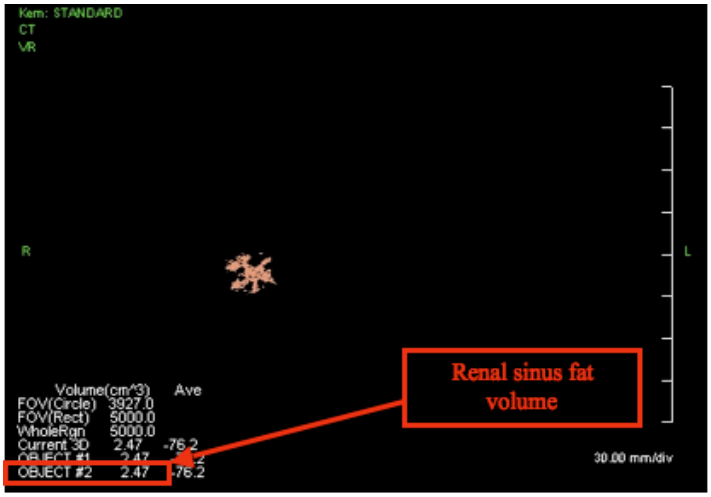


14) Under the **mask** tab, click the **3D** tab at the bottom of the screen. When selected, the fat accumulation within the renal sinus will be visualized in pink (**Protocol Figure 5**).

Protocol Figure 5: 3D visualization of fat within the renal sinus selected using this protocol.

15) Select **measure** and then **volume**. A set of measurements will appear on the lower left corner of the screen (**Protocol Figure 6**).

Protocol Figure 6: Volumetric measurement of renal sinus fat in the measurement slice.



a. The measurement for “Object #2” is the renal sinus fat volume in cubic centimeters (**Protocol Figure 6**).
b. If “Object #1” and “Object #2” do not appear in the output on the lower left of the screen, then the fat measurement is below the limit of detection. This value will be coded as 0.004 in the final dataset.

16) Select **output** at the top of the screen. After selecting **output,** if a picture is already present in the output window, delete it before proceeding to step 17.

17) Select **capture** on bottom left of screen.
18) Use the mouse to left-click on the image. This image will show up on the output screen after this left-click.

Select “**save file**” and save the file as a .jpg.