Obesity-related Renal Damage in Adolescent Women – BSA Matters

Dana Bielopolski[1], Neha Singh, Caroline S. Jiang[1], Robert MacArthur[1], Kimberly S. Vasquez[1], Dena Moftah[2], Roger Vaughan[1], Rhonda G. Kost[1], Jonathan N. Tobin[1,2]
[1]The Rockefeller University Center for Clinical and Translational Science, New York NY
[2]Clinical Directors Network (CDN), New York NY

Introduction: The obesity epidemic is becoming endemic in the US with significant increases in obesity and severe obesity with a linear trend from 1999 to 2016, in adolescent females ages 16 to 19 years (1). Recent data show a similar trend in both children and adults, with obesity increasingly contributing to renal injury and to an important increase in chronic kidney disease (2). Obesity-related glomerulopathy (ORG) has a stage manifested as hyperfiltration and albuminuria, which can be reversed if detected early(3). The formula currently used in clinical practice to approximate glomerular filtration rate (GFR) is adjusted to ideal body surface area (BSA)(4). This approach under-estimates filtration in obese individuals, obscures the detection of hyperfiltration and the opportunity to clinically intervene.

Aim: We sought to understand whether calculating absolute GFR improves estimation of early stages of ORG, a pathologic and potentially reversible process.

Cohort construction - De-identified electronic health record (EHR) data were extracted for female adolescents aged 12-21 years, who received health care services from 1/1/2011 to 12/31/2015 in NYC from 12 academic health centers and community health centers that are part of the PCORnet NYC Clinical Data Research Network (NYC-CDRN/INSIGHT(7)).

BMI and BSA calculations - BMI was calculated by dividing a person's weight in kilograms by the square of height in meters. BSA was calculated according to the metric Du-Bois formula(4). BMI-for-age values were classified according to the WHO reference data for BMI z-score(5) into the following categories:

Under weight =BMI <5th percentile, Normal weight = 5th percentile< BMI <85th percentile
Overweight = ≥BMI ≥85th percentile, Obesity = BMI ≥95th percentile.

eGFR calculation according to age (6) – ages 18-21 years - CKD-EPI formula, ages 12-18 years - revised Schwartz formula

Calculating absolute GFR. eGFR values were divided by 1.73 and multiplied by BSA to eliminate the normalized correction. This was carried for all subjects, irrelevant of the method used to create eGFR. **Statistical analysis:**

Analyses were performed using SAS (v 3.2.5). Nominal variables were expressed as numbers (%) in the descriptive analyses. Percentage comparisons of groups were performed using the chi-square test. Pearson's correlation was used Continuous variables were expressed as mean ± SD or median (minimum-maximum) and were compared using ANOVA including Tukey's approach for multiple comparisons. Alpha (2-tailed) = 0.05 was considered statistically significant.

Results: Exploring renal function across the cohort revealed similar creatinine values across very different BMI levels, and as a result similar eGFR, when the formulae used is adjusted to ideal BSA. At the same time, a subpopulation of the cohort showed different urine creatinine, creating a statistically significant trend across BMI groups, suggesting increasing hyperfiltration as body size increases.

When assessed by eGFR, hyperfiltration rates were similar between BMI groups, although these were statistically significantly different due to small number of participants. Calculating absolute GFR resulted in increasing rates of hyperfiltration across BMI groups in a manner that suggests obesity as a possible causative factor.

Table 1 – Demographic characteristics of patients included in the final cohort

Characteristic	Underweight (N=1,085)	Normal (N=11,971)	Overweight (N=4,353)	Obese (N=5,008)	Overall (N=22,417)	P-value
Age (years)	17±2.8	17±2.5	17±2.6	17±2.6	17.1±2.5	<.0001*
Height (cm)	157±10	159±8	160±8	161±8	160±8	<.0001
Weight (kg)	40±7	53±9	69±9	91±19	[illegible]	<.0001
BMI (kg/m^2)	16±1.4	21±2.3	27±1.8	35±6.1	25±4.2	<.0001
BSA (m^2)	1.3±0.2	1.5±0.2	1.7±0.2	1.9±0.2	1.7±1.7	<.0001
Race						
African American	299 (27.5%)	3,631 (30%)	1,467 (34%)	1,918 (38.2%)	7,315 (32.6%)	<.0001
Caucasian	224 (20.6%)	1,807 (15%)	448 (10%)	398 (7.9%)	2,877 (12.8%)	<.0001
Hispanic	380 (35.0%)	4,695 (39.2%)	1,881 (43.2%)	2,112 (42.1%)	9,068 (40.4%)	<.0001
Smoking	58 (6.1%)	791 (7.4%)	375 (8.6%)	454 (9.0%)	1,678 (8.4%)	<.0001
Systolic BP (mmHG)	102±11	105±11	110±11	115±13	109±12	<.0001
Diastolic BP (mmHG)	64.0±8	64.7±8	67±9	69±9	66±9	<.0001
Hemoglobin A1c(%)	5.6	5.6	5.6	5.6	5.6	0.052

Table 2 – Renal characteristics across BMI groups.

Characteristic	Underweight (N=1,085)	Normal (N=11,971)	Overweight (N=4,353)	Obese (N=5,008)	Overall (N=22,417)	P-value
Serum creatinine (mg/dl)	0.73±0.2	0.75±0.2	0.74±0.2	0.74±0.2	0.74±0.2	0.001*
Urine creatinine (G/24h)	0.57±0.3 (10)	0.95±0.4 (124)	1.17±0.4 (62)	1.26±0.5 (113)	1.09±0.4 (309)	0.001**
BSA standardized eGFR (ml/min/1.73m^2)	106±30	103±27	106±27	105±26	104±27	<.0001
Hyperfiltration BSA standardized eGFR	167 (15%)	1,445 (12%)	630 (15%)	667 (13%)	2,909 (13%)	<.0001
Absolute eGFR (ml/min)	82±26	92±26	105±29	119±33	100±31	<.0001
Hyperfiltration Absolute GFR	25 (2.3%)	728 (6.1%)	755 (17.4%)	1,568 (31.4%)	3,076 (14%)	<.0001

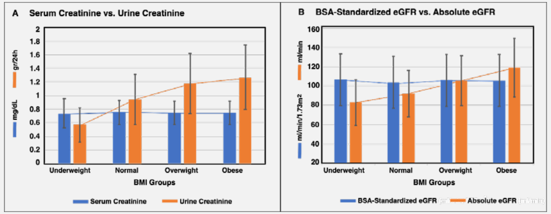

Figure 1- **Measured renal characteristics and inferred filtration rate according to the different formula**. **A** - serum creatinine (blue) vs. urine creatinine (orange) across BMI groups. **B** - eGFR according to CKD-EPI and Schwartz formula (blue) vs. absolute GFR according to CKD-EPI and Schwartz formula (orange)

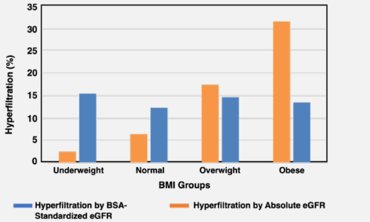

Figure 2 – **Hyperfiltration according to BMI group by eGFR (blue) vs. absolute GFR (orange).** Columns represent percent of subjects from the BMI group that crossed the threshold of 135ml/min, defined as hyperfiltration

Conclusions: Indexing GFR to BSA has little influence on GFR values in 'normal' body size patients, whereas, in obese patients, such indexing will lead to important, erratic and unacceptable underestimations of the 'true GFR' and obscure detection of hyperfiltration. Therefore, absolute noncorrected GFR should be preferred in daily practice and in clinical studies for the obese (and maybe the overall) population(9).

We suggest implementing a correction to the currently recommended formula, that will estimate absolute GFR rather than a normalized one. This change will improve primary care physicians' and pediatricians' ability to identify, intervene and prevent obesity-related renal damage in the vulnerable population of young adults(10).

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