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Effect of Weight Loss on Renal Function in Overweight and Obese Patients with Heart Failure

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Abstract

Aims—The effect of intentional weight loss on glomerular filtration rate (GFR) in overweight and obese patients with heart failure (HF), diabetes mellitus (DM) and/or metabolic syndrome (MS) has not been studied. The purpose of the present study is to assess the short term effects of intentional weight loss on renal function in this population.

Materials and Methods—Fifty nine patients were recruited to participate in a 3-month intensive behavioral weight management intervention and received one of two standard structured energy-restricted meal plans (1200 or 1500 kcal/day) based on their computed calorie deficit. Weight and renal function (serum creatinine, BUN and estimated glomerular filtration rate based

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on two formulas - Modification in Renal Disease Study (MDRD), and modified version of Cockcroft-Gault formula reported by Salazar Corcoran for obese patients (absolute and relative formulas) - were evaluated at baseline and at 3 months.

Results—Participants had eGFR in the normal range at baseline and lost an average of 7.56 ± 14.9 pounds ($p<0.0001$) over 3 months; however, there was no significant reduction in serum creatinine, BUN or eGFR.

Conclusion—This study provides evidence that intentional weight loss in overweight and obese patients with HF along with DM, and/or MS and normal baseline renal function does not adversely affect renal function overtime.

Keywords

Heart failure; renal function; hyperfiltration; obesity; weight loss

Introduction

With the obesity epidemic as a universal public health concern, many studies are underway to design and test weight loss interventions that result in loss of body fat without any deleterious effects. Since obesity may lead to and be associated with chronic kidney disease (CKD),[1;2] the effect of dietary interventions on the potential risk of increased renal disease is of outmost concern. A systematic review of patients with existing CKD revealed that only a few randomized trials have examined the effect of weight loss on CKD and these have shown beneficial effects of weight loss on renal function but authors state the evidence is still sparse.[3] A major challenge in preventing CKD lies in early detection of high risk patients. Glomerular filtration rate (GFR) is used as the best index of renal function by measuring the filtering capacity of the kidneys.[4;5] Since using radiolabeled exogenous markers to accurately measure GFR can be costly and time consuming, several formulas have been used to provide estimated GFR (eGFR) based on serum creatinine levels. Currently, renal function is assessed best by eGFR, as serum creatinine is an unreliable marker of kidney function.[6;7] The most widely used and validated formulas to calculate eGFR are the Modification of Diet in Renal Disease (MDRD)[8] and a modified version of Cockcroft-Gault formula reported by Salazar Corcoran.[9] The MDRD formula (which incorporates age, gender, and serum creatinine) has been widely used in various investigations including a study of obese individuals without overt kidney disease,[10] in overweight and obese Malaysian subjects,[11] and in a weight management study comparing very low vs. high carbohydrate diet.[12] However, the validity of different measures of eGFR to assess CKD in obese patients has had conflicting reports.[3;13;14] A modification of the Cockcroft-Gault formula has been developed by Salazar and Corcoran which has been validated in obese patients.[9] In the present study, we will compare the eGFR obtained at baseline using the MDRD and Salazar-Corcorian (absolute and relative) formulas to those estimated at 3 months following a weight loss regimen. This is a first report of eGFR in overweight and obese patients with HF, DM, and/or MS with the primary aim to assess the short term effects of intentional weight loss on renal function (serum creatinine, blood urea nitrogen [BUN] and eGFR). As a secondary aim, we will examine the relationship between

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weight, waist circumference, and body composition on eGFR by two methods described herein.

Materials and Methods

The enrollment criteria and study design have been described elsewhere.[15] Briefly, 59 participants were recruited and provided informed consent to participate in a randomized clinical trial for overweight and obese patients with HF, DM, and/or MS (Table 1). University of California Los Angeles and University of California Irvine Institutional Human Subjects Review Committees approved the study. Participants who met the inclusion exclusion criteria[15] received a 3 month behavioral weight management intervention based on energy-restricted meal plans (1200 or 1500 kcal/day) which would provide a calorie deficit aimed at 500kcal or more. They reported to the study centers at 2 weeks, 4 weeks, 8 weeks and 12 weeks to meet with a nutrition counselor and review goals and plans described in a "Participant Handbook".

For the purpose of this descriptive study, weight, body composition, physical and clinical characteristics were compared at baseline vs. 3 month visits. Estimated GFR was derived by two formulas where age is measured in years, creatinine in mg/dL, weight and height (where needed) in kilograms and meters, respectively.

MDRD formula

$$\text{Estimated glomerular filtration rate (eGFR) } (\text{mL}/\min/1.73\,\text{m}^2) = 186.3 \times (\text{serum creatinine}[\text{mg/dL}])^{-1.154} \times (\text{age})^{-0.203} \times 0.742\ (\text{if female}).$$

Salazar-Corcoran formula

For men:

$$\text{eGFR } (\text{mL}/\min) = (137 - \text{age}) \times [(0.285 \times \text{weight}) + (12.1 \times \text{height}^2)]/(51 \times \text{serum creatinine})$$

For women:

$$\text{eGFR } (\text{mL}/\min) = (146 - \text{age}) \times [(0.287 \times \text{weight}) + (9.74 \times \text{height}^2)]/(60 \times \text{serum creatinine})$$

. Relative eGFR by the Salazar-Corcoran formula were calculated by normalizing for body surface area (BSA) and expressing the eGFR as mL/min/1.73 m^2 where $\text{BSA } (\text{m}^2) = [\text{weight (kg)}]^{0.425} \times [\text{height (cm)}]^{0.725} \times 0.007184$.

Data was analyzed using SPSS version 19.0 for Windows. Sociodemographic and clinical variables were computed using descriptive statistics (e.g., means and standard deviations for continuous variables and Pearson $\chi 2$ tests for categorical variables). Changes in renal function, weight, waist circumference, and body composition (e.g., lean mass, percent fat) from baseline to 3 months were analyzed using independent two sample t-tests. The relationships between variables of interests were evaluated using Pearson Moment Correlations and Spearman Rho depending on level of measurement.

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Results

Participant characteristics

Table 1 shows the sociodemographic and clinical characteristics of the study sample. Participants ranged in age from 27 to 81 and were on the average moderately obese (body mass index [BMI], 36.59 ± 6.22 kg/m^2). Participants' baseline clinical characteristics including fasting blood glucose, cholesterol, BUN, creatinine and blood pressure measurements are also shown in Table 1.

Changes in clinical status post intervention

Statistically significant changes in weight, waist circumference, and lean mass were noted from baseline to 3 months (Table 2, all p's < 0.005). However, the serum creatinine and BUN remained unchanged over time. Likewise, serum creatinine driven formulas of MDRD, and absolute and relative (normalized for body surface area) Salazar-Corcoran formula did not change significantly over time.

Association between eGFR and weight and body composition

The correlation matrix for key variables is illustrated on Table 3. Data show that the eGFR by MDRD formula was significantly correlated with BMI and total % body fat, and the eGFR by absolute Salazar-Corcoran formula was significantly correlated with weight, BMI, waist circumference and total % body fat. The relationships were not observed once a correction was made for body surface area eGFR (Salazar-Corcoran, normalized); this finding is intuitive since this formula takes into account changes that would be expected secondary to changes in body weight.

Discussion

To our knowledge, this is the first study to explore the effect of intentional weight loss on renal function in overweight and obese patients with HF who also have DM and/or MS. Obesity is one of today's most pressing health issues worldwide, and is believed to lead to health consequences including coronary heart disease, hypertension, DM, dyslipidemia, sleep apnea, and certain cancers.[16] Furthermore, being overweight or obese and or having DM are all risk factors for CKD.[2;17–19] The present population of overweight and obese patients with HF, DM, and/or MS are potentially vulnerable and at risk for renal damage.

In order to elucidate the effect of intentional weight loss on changes in renal status, we enrolled overweight or obese patients with normal kidney function (as evaluated by baseline creatinine levels). As an addition to the well-known MDRD equation for estimating GFR, Salazar and Corcoran's equation (which is a modification of Cockcroft-Gault formula),[9] was utilized to measure eGFR at baseline and 3 months. Our findings show that serum creatinine, BUN, and eGFR (estimated using both methods) did not change over 3 months despite a change in weight and BMI. The present results are in agreement with previous studies of short term weight loss interventions (24 or 52 weeks) that reported no differences in serum creatinine and eGFR (estimated by MDRD) in overweight or obese participants with or without type-2 DM.[12;20;21] It is important to note that in all these studies (present one

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included), participants were selected based on the absence of any preexisting renal insufficiencies (indicated by low eGFR of >60 ml/min/1.73 m^2 defined by the Kidney Disease Outcome Quality Initiative Guidelines).[22] Thus, the lack of any effect of short term weight loss on renal function is only valid in those with preserved renal function; the effect of weight loss on overweight or obese HF patients with compromised kidney function warrants further investigation.

Our findings indicate that absolute values of eGFR (by MDRD and Salazar methods) were significantly correlated with BMI and percent body fat; however, these relationships were not observed in the Salazar equation modified for BSA. Since serum creatinine is produced by muscle tissue, changes in muscle mass can affect eGFR and confound the conclusions regarding renal function. Our results reflected a significant reduction in average lean mass. Correcting for BSA was important to clearly indicate a lack of change in eGFR with intentional weight loss. In clinical settings, BSA has been described as a better indicator of metabolic mass than body weight because it is less influenced by changes in mass of fatty tissue.[23] The mean values of eGFR estimated by both methods (MDRD and Salazar absolute or relative) were in the normal range (defined by National Kidney Foundation of > 60 mL/min/1.73 m^2). However, whether the eGFR were accurate can only be verified by in vivo isotopic renal clearance methods which are cumbersome and expensive. Estimated GFR relying on formulas based on serum creatinine and/or cystatin C remain controversial in clinical research particularly in obese individuals and are especially flawed with respect to weight loss due to alterations in body composition.[24] Furthermore, a very recent study showed that the association between weight change and renal function reflected a wide variation based on the method of assessment.[25] The effect of increased weight with increase in systemic arterial pressure and increase renal plasma flow and eGFR are well documented[26;27] such that a reduction in weight is anticipated to result in a decrease in absolute eGFR or a reduction in obesity related glomerular hyperfiltration.[28]

The present report shows a trend toward decreasing values for eGFR (absolute or relative to BSA) but the changes were not statistically significant. Since the study was only 12 weeks in length, it is possible that the changes may approach significance over longer period of time and with possible further changes in weight. There was not a randomized concurrent control group not exposed to the intentional weight loss intervention. Another limitation of the current study is the small sample size. The eGFR data for those that did not complete the study and the average results for a larger sample of overweight and obese patients with HF, DM and/or MS are needed to better delineate the effect of intentional weight loss on renal function.

Conclusion

The results of this study provide evidence that intentional weight loss in overweight and obese patients with HF along with DM, and/or MS and normal baseline renal function does not adversely affect renal function over a 3 month behavioral weight management program. Future studies are warranted to examine the effect of macro and micro nutrients on the changes in risks associated with renal function over short and long term durations in this highly vulnerable population.

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Table 1

Sociodemographic and Clinical Characteristics (N = 59)

	Baseline All Subjects
Age, years (Mean ± SD)	58.73 + 9.47
Male (%)	71.2%
White (%)	49.2%
History of Diabetes	37.3%
History of Hypertension	50.8%
History of Smoking	47.5%
History of Statin use	50.8%
NYHA class, N (%)	
Class 2	79.8%
Class 3	18.6%
Weight (lbs)	238.11 + 46.69
Fasting Glucose (mg/dl)	129.87+ 56.17
Total cholesterol	157.45 + 46.91
LDL	90.47 + 35.83
HDL	40.93 + 12.07
Triglycerides	148.11 + 72.02
BUN (mg/dL)	20.35 + 8.08
Creatinine (mg/dL)	1.088 + 0.28
SBP	119.80 + 19.90
DBP	72.56+ 11.76

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Table 2

Changes in Weight and body composition and estimation of glomerular filtration rate after 3 months of behavioral weight management intervention (N = 59)

	Baseline	3 Months	p
Weight (Pounds)	238.11 + 46.69	230.55+ 45.00	0.000
BMI (kg/m^2)	36.59 + 6.22	34.87 + 5.06	0.002
Waist Circumference (cm)	47.04 + 4.28	45.52 + 4.26	0.001
Lean Mass (kg) (DEXA)[a]	61.96 + 9.54	58.92 + 12.53	0.026
Total % Fat (DEXA)[a]	37.66 + 1.08	37.27 + 1.09	0.608
BUN (mg/dL)	20.35 + 8.08	21.067 + 9.02	0.140
Serum Creatinine	1.088+ 0.277	1.115 + 0.317	0.430
eGFR (MDRD) (ml/min/1.73m^2)[b]	77.84 + 25.98	77.06 + 29.23	0.803
eGFR (Salazar-Corcoran)[c]	98.51 + 34.16	94.12 + 41.05	0.212
eGFR (Salazar-Corcoran) (mL/min/1.73 m^2)[d]	81.71 + 30.38	77.63 + 77.63	0.479

[a]DEXA (dual-energy X-ray absorptiometry)

[b]eGFR (estimated by MRDR-Modification in Renal Disease Study)[8]

[c]eGFR (estimated by Salazar-Corcoran formula)[9]

[d]eGFR (Salazar-Corcoran formula normalized for body surface area BSA.

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Table 3

Correlational Matrix of Key Variables of Interest at Baseline (N = 59)

	1	2	3	4	5	6	7	8
1. Weight								
2. BMI	0.813**							
3. Waist Circumference	0.798**	0.732**						
4. Lean Mass	0.521**	0.189	0.405**					
5. Percent Body Fat	0.153	0.561**	0.327**	−0.482**				
6. eGFR (MDRD)	0.209	0.346**	0.177	−0.111	0.348**			
7. eGFR (Salazar)	0.573**	0.556**	0.380**	0.162	0.277*	0.876**		
8. eGFR (Salazar-Normalized to BSA)	−0.102	−0.072	−0.057	−0.126	−0.021	0.129	0.086	

** Correlation is significant at the 0.01 level (2-tailed)

* Correlation is significant at the 0.05 level (2-tailed)