

## Effect of Dietary Energy Intake on Risk Factors for Coronary Artery Disease with the Focused on Serum Creatinine Concentration

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**Abstract:** Advantages or disadvantages of calorie restriction as a factor for reducing Coronary Artery Disease (CAD) risk factors have been questioned. In the present study, researchers examined the effects of a short-term dietary calorie intake on laboratory parameters related to the risk factors for CAD, especially serum creatinine rise in patients with CAD. In a cross-sectional study, 444 consecutive patients with the diagnosis of CAD and candidate for coronary artery bypass surgery were participated in this study. Laboratory parameters as CAD risk factors were measured. Energy intake was estimated from the self recorded dietary intake records so that the energy content of the entire diet is computed as the sum of the energy available in each food item consumed. Linear regression analysis showed no significant relationships between dietary energy intake and laboratory parameters of fasting blood glucose, lipoprotein and lipid profiles, however in both obese and non-obese groups, there were adverse relationships between dietary energy intake and last serum creatinine. In multivariate analysis, after adjusting for confounders, significant adverse relationship was found between dietary energy intake and serum creatinine concentration.

**Key words:** Coronary artery disease, energy intake, creatinine, risk factor, lipoprotein

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### INTRODUCTION

Poor outcome and morbidity associated with the progression of Coronary Artery Disease (CAD) is strongly related to the abnormality of metabolic systems that can be powerfully influenced by nutritional regimens. Several studies could indicate that the appropriate dietary changes decreased arteriosclerotic plaque formation, improve endothelial vasomotor dynamics, reduce oxidation of low-density lipoproteins and enhance thrombolytic activity (Hunt *et al.*, 1995). However, advantages or disadvantages of calorie restriction as a factor for reducing CAD risk factors have been questioned. Some studies have been shown that low-calorie diet directly inhibits sympathetic activity which suggests that the decreasing of sympathetic activity can lead to the control of hypertension as a major risk factor for CAD (Landsberg and Young, 1978; O'Dea *et al.*, 1982; Andersson *et al.*, 1991; Grassi *et al.*, 1994, 1998; Iwane *et al.*, 2000). Furthermore, it has been demonstrated that the weight reduction with calorie restriction can improve glucose and lipid metabolisms which led to a substantial reduction in the cardiovascular risk profile, especially in obese patients (Uusitupa *et al.*,

1990). In addition, the data have been suggested that low-calorie diet can prevent cardiovascular tissues from oxidative stress provoked by diabetes mellitus that has been known as a main predictor for high CAD-related morbidity and mortality (Minamiyama *et al.*, 2007). Besides, some other clinical and experimental studies have been highlighted the complications of calorie restriction in CAD patients. Cardiac structure and myocardial contractility were affected during calories restriction so that it could increase myocardial hydroxyproline concentration and led to left ventricular eccentric remodeling and diastolic dysfunction (Cicogna *et al.*, 2001; Okoshi *et al.*, 2001). Also in another study, low-calorie diet caused systolic ventricular dysfunction and diastolic dysfunction probably due to a reduction in myocardial elasticity (Okoshi *et al.*, 2004). Besides, the effects of energy intake on renal function and serum creatinine concentration have not been clearly determined. In a study by Huidobro *et al.* (2001), it was showed that the patients with chronic renal failure and in chronic dialysis have a high prevalence of caloric malnutrition, which may be due to a poor caloric intake. Also, it has been recommended that low energy intake should be considered, prevented and treated as

possible in persons with clinically important renal insufficiency (Garg *et al.*, 2001). Researchers believed that more studies are needed to determine the effects of low-calorie diet on the progression or prevention of risk factors for CAD, especially renal failure and creatinine abnormalities, as a main predictor for poor outcome in patients with acute coronary syndrome (Walsh *et al.*, 2002; Li *et al.*, 2006; Latchamsetty *et al.*, 2007; Wannamethee *et al.*, 1997). In the present study, researchers examined the effects of a short term dietary calorie intake on laboratory parameters related to the risk factors for CAD, especially serum creatinine rise in patients with CAD.

## MATERIALS AND METHODS

**Study population:** In a cross-sectional study, 444 consecutive patients with the diagnosis of CAD and candidate for coronary artery bypass surgery were participated in this study. Participants' demographic characteristics, clinical information and diagnostic data were collected by the review of clinical recorded files. In this study, CAD was considered significant if there was a 75% or greater stenosis in the cross-sectional diameter and 50% or greater stenosis in the luminal view (Tavakoli *et al.*, 2002). All subjects gave informed consent before their participation.

**Laboratory measurements:** Blood samples were drawn from the corresponding peripheral vein into vacutainer tubes after 12-14 h of overnight fasting. Plasma glucose concentrations were assessed by means of a glucose hexokinase method (Pars Azmoon kits accredited by Bioactiva Diagnostica, Germany). Serum total cholesterol, HDL cholesterol and triglycerides were measured via enzymatic techniques (Pars Azmoon kits accredited by Bioactiva Diagnostica, Germany). The Friedewald formula was used to calculate Low Density Lipoprotein (LDL) cholesterol, except when the triglyceride level was  $>4.52 \text{ mmol L}^{-1}$ .

Blood pressure was calculated as the mean of two measurements, performed in the sitting position after 5 min of rest, using a random-zero sphygmomanometer (Hawksley-Gelman, Lancing, Sussex, UK). C-Reactive Protein (CRP) level was measured by immunoturbidometry (Pars Azmun, Iran) and lipoprotein (a) was measured using Tint ELIZA (Biopool, USA). Creatinine was measured with Jaffe reaction (Parsazmon Kit, Tehran, Iran) using an autoanalyzer (Hitachi, Tokyo, Japan).

**Energy intake:** Studied patients were interviewed at admission to surgical ward and before operation and asked to report how often they consumed each of the food items listed as the number of times per day, per month or per year during the previous year. Nutritional assessment was obtained by a validated semi-quantitative Food Frequency Questionnaire (FFQ), previously validated in Iran (Malekshah *et al.*, 2006) and a 24 h dietary recall questionnaire to record the types, amounts and frequencies of foods consumed. Each food item was coded from a descriptive list in a food database that uses an average value for the nutrient content. Energy intake was estimated from the self recorded dietary intake records. The energy content of the entire diet is computed as the sum of the energy available in each food item consumed.

**Statistical analysis:** Results were reported as mean $\pm$ Standard Deviation (SD) for quantitative variables and percentages for categorical variables. Continuous variables were compared using independent t-test or one-way Analysis of Variance (ANOVA). Multivariate linear regression analysis was used to investigate the potential confounding effects on the association between dietary energy intake and serum creatinine concentration. p-values of 0.05 or less were considered statistically significant. All the statistical analyses were performed using SPSS version 13.0 (SPSS Inc., Chicago, IL, USA).

## RESULTS

Demographic characteristics, clinical data and laboratory parameters of studied patients are summarized in Table 1 and 2. Mean age of studied patients was 58.47 (ranged 38-80 years) and more than two third of them were male. The most common general risk factors for CAD included hypercholesterolemia (69.8%), hypertension (48.2%) and family history of CAD (45.5%). Among studied patients, 23% were obese with the body mass index  $32.57 \pm 2.46 \text{ kg m}^{-2}$  (ranged 30.0-40.0  $\text{kg m}^{-2}$ ). In the review of angiographic reports, it was found that the majority of patients suffered from three coronary vessels disease.

Linear regression analysis showed no significant relationships between dietary energy intake and laboratory parameters of fasting blood glucose, lipoprotein and lipid profiles (Table 3), however in both obese and non-obese groups, there were adverse relationships between dietary energy intake and last serum creatinine. In multivariate analysis, after adjusting for confounders, significant adverse relationship was found between dietary energy intake and serum creatinine concentration (Table 4).

Table 1: Demographic characteristics and clinical data of studied patients (n = 444)

Variables	Values
Male (gender)	344 (77.5)
Age (year)	58.47±8.90
Body mass index (kg m <sup>-2</sup> )	27.15±3.88
<b>Education level</b>	
Primary	229 (51.6)
Secondary	139 (31.3)
Higher	76 (17.1)
Family history of CAD	202 (45.5)
Current cigarette smoking	162 (36.5)
Opium addiction	63 (14.2)
Alcohol using	60 (14.4)
Hypercholesterolemia	310 (69.8)
Hypertension	214 (48.2)
Cerebrovascular disease	17 (3.8)
Peripheral vascular disease	109 (24.5)
Recent myocardial infarction	224 (50.6)
Renal failure	36 (8.1)
Ejection fraction (%)	49.13±9.92
<b>Functional class</b>	
I	160 (36.0)
II	224 (50.5)
III	60 (13.5)
Euroscore	2.15±2.10
<b>Coronary vessels involvement</b>	
Single-vessel disease	18 (4.1)
Two-vessel disease	94 (21.2)
Three-vessel disease	332 (74.8)

CAD: Coronary Artery Disease

Table 2: Laboratory parameters of studied patients (n = 444)

Variables	Values
Last fasting blood sugar (mg dL <sup>-1</sup> )	106.57±32.76
Last creatinine (mg dL <sup>-1</sup> )	1.25±0.250
Triglyceride (mg dL <sup>-1</sup> )	171.11±87.77
Cholesterol (mg dL <sup>-1</sup> )	159.46±42.73
High density lipoprotein (mg dL <sup>-1</sup> )	40.39±8.450
Low density lipoprotein (mg dL <sup>-1</sup> )	86.67±39.50
Hemoglobin A <sub>1c</sub> (%)	6.02±1.760
Albumin (gdL <sup>-1</sup> )	4.65±0.320
Lipoprotein (a) (mg dL <sup>-1</sup> )	31.76±26.87

Table 3: Relationships between energy intake and laboratory parameters related to CAD risk factors in obese (n = 102) and non-obese (n = 342) patients

Parameters	Obese patients			Non-obese patients		
	Standardized β	R <sup>2</sup>	p-value	Standardized β	R <sup>2</sup>	p-value
Last fasting blood sugar	0.108	0.012	0.279	0.006	0.000	0.915
Triglyceride	0.131	0.017	0.189	-0.012	0.000	0.821
Cholesterol	0.129	0.017	0.197	0.015	0.000	0.776
High density lipoprotein	0.153	0.023	0.125	0.075	0.006	0.164
Low density lipoprotein	0.050	0.002	0.621	0.016	0.000	0.772
Lipoprotein (a)	-0.003	0.000	0.426	-0.043	0.002	0.426
Last creatinine	-0.197	0.039	0.046	-0.114	0.013	0.034

## DISCUSSION

Majority of previous studies focused on the effects of protein intake on the outcome of patients with renal failure and undergoing dialysis. However according to

Table 4: Multivariate analysis of the effects of dietary energy intake on serum creatinine concentration adjusted for confounders

Variables	Univariate p-value	Multivariate analysis	
		Standardized β	p-value
Dietary energy intake	0.005	-0.138	0.002
Male gender	<0.001	0.330	<0.001
Advanced age	0.003	0.166	<0.001
Hypercholesterolemia	0.102	0.007	0.871
Peripheral vascular disease	0.105	-0.038	0.401
Recent myocardial infarction	0.079	0.013	0.783
Ejection fraction	0.064	-0.039	0.398

R<sup>2</sup> = 0.161

the role of renal function, as a predictor for poor outcome of patients with acute coronary syndrome or patients undergoing cardiac surgeries, assessment of relationship between dietary energy intake and CAD risk factors, especially renal dysfunction is necessary. The present study is the first study that evaluate this relationship in CAD patients who candidate for coronary artery bypass surgery. The study showed that after adjusting for confounders, adverse relationship was found between dietary energy intake and serum creatinine concentration in CAD patients. In a recent study by Huang *et al.* (2008), low energy intake was significantly positively correlated with elevations in creatinine and BUN. Their study hypnotized that lower energy intake may be associated with deteriorating renal function (Huang *et al.*, 2008). Furthermore in some studies, it was indicated that daily energy intake in patients with chronic kidney disease was lower than recommended and this reduction could be related with the outcome of these patients (Fassett *et al.*, 2007; Kopple, 1998; Ratsch *et al.*, 1992). Also, it has been emphasized that nutritional abnormalities has been frequently found, even in apparently clinically stable patients on chronic renal failure and even caloric rather than protein undernutrition has been the major abnormality of their wasting (Lorenzo *et al.*, 1995). In a study for determination of the effects of energy intake on progression of induced chronic renal failure in cats, it was shown that diets replete in calories were associated with mild increase of nonglomerular lesions (Finco *et al.*, 1998). Also, Kopple *et al.* (1986) showed that a dietary intake >30 kcal/kg/day may be more likely to maintain neutral or positive nitrogen balance, maintain or increase body mass and reduce net urea generation in non-dialyzed patients with chronic renal failure.

It seems that the two mechanisms can be hypnotized to explain the influence of low energy intake on creatinine raise. Firstly according to the results of the previous studies, adequate energy intake is necessary to maintain nitrogen balance and creatinine concentration (Haung *et al.*, 2008; Kopple *et al.*, 1986). In addition, the

role of nitrogen imbalance as a predictor for the progression of CAD has been observed so that among patients with unstable coronary syndromes, an elevated BUN has been associated with increased mortality and independent of serum creatinine-based estimates of GFR (Kirtane *et al.*, 2005; Santopinto *et al.*, 2003). Therefore, researchers believed that low energy intake can disturb nitrogen balance and lead to the renal dysfunction and serum creatinine raise and thus can influence the outcome of CAD patients. Also, it was clearly shown that the inflammatory processes is associated with increased energy expenditure in patients with kidney disease (Utaka *et al.*, 2005) and therefore can be lead to the increase of creatinine concentration. Moreover, the inflammatory mechanisms of CAD progression and severity have been previously described (Wilson, 2008; Abou-Raya and Abou-Raya, 2006). Therefore in the patients with CAD, underlying inflammation may increase energy expenditure and increase creatinine concentration.

Totally according to the importance of the control and prevention of renal dysfunction and creatinine abnormality, as main predictors for CAD, regulation of energy intake in these patients can be a potential protocol for the control of these predictors and prevention of adverse outcome of CAD.

### CONCLUSION

There was adverse relationship between dietary energy intake and serum creatinine concentration in CAD patients. Regulation of energy intake in these patients can be a potential protocol for the control of these predictors and prevention of adverse outcome of CAD.

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