RESEARCH ARTICLE

Red meat intake, insulin resistance, and markers of endothelial function among Iranian women

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Scope: Few data, with conflicting findings, are available linking red meat consumption to indicators of insulin resistance and endothelial dysfunction. This study aimed to investigate the association of red meat consumption with insulin resistance and endothelial dysfunction among a sample of female nurses in Isfahan, Iran.

Methods and results: This cross-sectional study was carried out among 420 female nurses who were selected by a multistage cluster random sampling method. Usual dietary intakes were assessed using a validated food frequency questionnaire. Red meat intake was calculated by summing up the consumption of all kinds of red meat in foods and processed meat in sausages and fast foods. To measure serum concentrations of adhesion molecules and glycemic indexes, a fasting blood sample was taken. After adjustment for potential confounders, high red meat intake was significantly associated with higher fasting plasma glucose, homeostasis model assessment of insulin resistance, and lower quantitative insulin sensitivity check index. Although high red meat intake was significantly associated with higher serum insulin levels and lower homeostasis model assessment of beta-cell function in the crude model, after controlling for BMI, the association was no longer significant. Red meat consumption was associated with high concentrations of E-selectin, soluble vascular cell adhesion molecule-1 (sVCAM-1), and soluble intercellular adhesion molecule-1 (sICAM-1) after adjustment for different potential confounders.

Conclusion: We found that increased red meat intake was associated with high concentrations of plasma endothelial dysfunction biomarkers and abnormal glucose homeostasis among Iranian women. Prospective studies are required to confirm these findings.

Keywords:
Endothelial function / Insulin resistance / Red meat

1 Introduction

Endothelial dysfunction is involved in the etiology of atherosclerosis, insulin resistance, and diabetes [1–3]. Experimental studies have shown that endothelial dysfunction contributes to the pathogenesis of coronary heart disease [3]. The association of endothelial dysfunction with some cancers has also been documented [4]. On the other hand, insulin resistance is fundamental to the etiology of type 2 diabetes and is linked to a wide range of diseases [5–10].

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Abbreviations: **FFQ**, food frequency questionnaire; **HOMA**, homeostasis model assessment; **sICAM-1**, soluble intercellular adhesion molecule-1; **sVCAM-1**, soluble vascular cell adhesion molecule-1; **QUICKI**, quantitative insulin sensitivity check index

Recent evidence has indicated that high consumption of red meat, particularly processed meat, may contribute to the development of metabolic syndrome [11], hypertension [12], stroke [13], and type 2 diabetes [2, 14]. Reduced consumption of red and processed meat has been recommended as a way to lower the risk of coronary heart disease [3, 15]. The biologic mechanisms underlying these relations are not entirely understood. The effect of red meat intake on these chronic conditions might be mediated through its effect on circulating inflammatory biomarkers and endothelial dysfunction. Additionally, the relationship between red meat intake and insulin resistance might play a role in the incidence of these conditions.

Few data, with conflicting findings, are available linking red meat consumption to indexes of insulin resistance and endothelial dysfunction. In a recent study [16], greater red meat intake was associated with elevated concentrations of inflammatory and glucose metabolic biomarkers in diabetes-free women. In a clinical trial study [17], consumption of red meat for 8 wk resulted in a significant increase in soluble vascular cell adhesion molecule-1 (sVCAM-1) and soluble intercellular adhesion molecule-1 (sICAM-1) levels and a reduction in insulin sensitivity. However, some studies have demonstrated no significant association between varying amounts of red meat intake and indexes of insulin resistance or endothelial dysfunction [18–20]. In a study by Clifton et al [20], adherence to a diet with high contents of red meat for 12 wk led to a fall in plasma glucose and insulin levels.

Almost all earlier studies on the association of red meat consumption with insulin resistance and endothelial dysfunction were done in developed countries and limited data are available from settings in developing nations. Assessing the link between red meat and insulin resistance and endothelial dysfunction is particularly relevant for Middle Eastern populations, because of their increased consumption of red and processed meats in recent years following the nutrition transition. On the other hand, prevalence of cardiovascular disease, atherosclerosis, diabetes, metabolic syndrome, and other chronic conditions has also increased in these countries in recent decades [21–23]. Given the positive relation between high consumption of red meat and these chronic conditions, studying the relation between red meat intake and insulin resistance and endothelial dysfunction might provide additional information to the field of diet–disease relations. This study aimed to investigate the association of red meat consumption with insulin resistance and endothelial dysfunction among a sample of female nurses in Isfahan, Iran.

2 Participants and methods

2.1 Study procedure and subjects

This cross-sectional study was conducted among a representative sample of Isfahani female nurses aged >30 years, who were selected by a multistage cluster random sampling method. Seven hospitals considering the number of public and private hospitals were randomly selected. From female nurses working in these hospitals, 510 individuals were invited to participate in this study and 480 women agreed to do so. We excluded women with a prior history of cardiovascular disease, diabetes, cancer, and stroke ($n = 26$), or infection ($n = 7$). In addition, those who had left ≥70 items blank on the food frequency questionnaire (FFQ, $n = 2$), or reported a total daily energy intake outside the range of 800–4200 kcal ($n = 9$), or those who were taking medications affecting glucose homeostasis were excluded ($n = 16$). After these exclusions ($n = 60$), the current analysis was done on 420 nurses. Written informed consent was obtained from each participant. The bioethics committee of Food Security Research Center, Isfahan University of Medical Sciences, in conjunction with the research council of Lorestan University of Medical Sciences, Iran, approved the study protocol.

2.2 Assessment of dietary intakes

Usual dietary intakes were assessed using a self-administered validated 106-item dish-based semi-quantitative FFQ [24]. The FFQ contained information on frequency of consumption of foods or dishes over the last year, along with common portion sizes used in Iran. The FFQ was validated among a subsample of 200 randomly selected participants. The reliability of the FFQ was assessed by comparing dietary intakes estimated by responses to the FFQ on two different occasions. Validity of the FFQ was assessed using the three 24-h dietary recalls as gold standard. Overall, these data indicated that the FFQ provides reasonably valid and reliable measures of the average long-term dietary intakes; for instance the correlation coefficient for reliability of red meat intake was 0.77 and for validity of red meat intake was 0.63. In the present study, total red meat consumption was calculated by summing up the consumption of all kind of red meat in different foods and processed meat in sausage and fast foods.

2.3 Assessment of biomarkers

To quantify serum concentrations of insulin, blood glucose, and adhesion molecules (E-selectin, sICAM-1, and sVCAM-1), a fasting (>12 h) blood sample was taken. The blood sample was then centrifuged within 30–45 min of collection and serum was frozen at −70°C until analysis. Measurement of adhesion molecules was done using available commercial kits by ELISA method (Biosource International and Bender Med Systems). The sensitivity of the assays for sICAM-1, sVCAM-1, and E-selectin were 0.6, 2.3, and 0.3 mg/L, respectively. Inter- and intraassay CVs for all biomarkers were <10%. Fasting plasma glucose was measured on the day of blood collection with an enzymatic colorimetric method using glucose oxidase. Measurement of serum insulin was done by ELISA method (Bender Med Systems). Insulin resistance

and sensitivity were estimated using the homeostasis model assessment (HOMA) and the quantitative insulin sensitivity check index (QUICKI), respectively.

2.4 Assessment of other variables

Weight was measured using digital scales while participants were wearing light clothes, without shoes and recorded to the nearest 0.1 kg. Height measurement was made while subjects were standing in a normal position without shoes by means of a tape measure. BMI was calculated as weight (kg) divided by height squared (m^2). Daily physical activity was assessed using the short form of International Physical Activity Questionnaire [25] and was expressed as MET-hours per week. Socioeconomic status was defined based on educational level, income, family size, being owner of a house or renting a house, house area, being owner of a car, number of cars and their type, and number of bedrooms in house. Additional covariate information regarding age, smoking habits, marital status, menopausal situation, medical history, and current use of medications and supplements was obtained using self-administered questionnaires.

2.5 Statistical methods

First, we calculated energy-adjusted red meat intakes using the residual method [26]. Energy-adjusted intakes were used to categorize participants into tertiles. One-way analysis of variance with Tukey's post hoc test and Pearson's chi-square test were used for comparing continuous and categorical data, across tertiles of red meat intake, respectively. Analysis of covariance (ANCOVA) was used to analyze dietary intake data that were age and energy intake adjusted. We used logarithmically transformed values of adhesion molecules in all statistical analyses due to the skewness in the distribution of these variables. Geometric means for serum concentrations of adhesion molecules across tertiles of red meat intake were computed using ANCOVA in different models. The covariates were chosen based on earlier publications. Adjustments for age, total energy intake (kcal/day), physical activity (MET-h/wk), current corticosteroid use (yes or no), oral contraceptive use (yes or no), marital status (single, married, divorced, and widow), menopausal status (yes or no), systolic blood pressure, diastolic blood pressure, and socioeconomic status (low, medium, and high socioeconomic status) were done in the first statistical model. Further statistical adjustment was made for intakes of refined and whole grains, fruits, vegetables, white meat, low- and high-fat dairy and percentage of energy from fat, nuts, and legumes in the second model. Additional adjustments for BMI were performed in the third model. For glucose metabolism indexes, additional adjustments for endothelial dysfunction were performed in the last model to test the hypothesis that the effect of red meat intake on insulin resistance is mediated through endothelial dysfunction. Finally, for serum concentrations of adhesion molecules, we added fasting plasma glucose, serum triglyceride, and serum total cholesterol, low-density lipoprotein, and low density lipoprotein cholesterol concentrations (all as continuous) into the model. The *p*-linear trend across increasing categories of red meat intake was obtained from linear regression analysis of adhesion molecules and glycemic indexes on a categorical variable of red meat intake. The stability of the models was considered to be disturbed by the multicolinearity if tolerance was <0.1. Tolerance is a statistic used to determine how much the independent variables are linearly related to one another. It is calculated as $1 - r^2$ for an independent variable when it is predicted by the other independent variables already included in the analyses. All statistical analyses were done using SPSS (SPSS, version 18, Chicago, IL). *p*-Values less than 0.05 were considered to be statistically significant.

3 Results

General characteristics of study participants by tertiles of red meat intake are presented in Table 1. Red meat intake tended to be associated with increased weight, BMI, and systolic blood pressure. In addition, those in the highest tertile of red meat intake tended to be current corticosteroid and OCP users and of high socioeconomic status than those in the lowest tertile. Totally, no significant difference was seen in terms of all covariates across tertiles of red meat intake. The distribution of individuals in terms of menopausal status, marital status, and prevalence of overweight or obesity were not significantly different across tertiles of red meat intake.

Dietary intakes of study participants across tertiles of red meat intake are shown in Table 2. High consumption of red meat was associated with greater intakes of fat, polyunsaturated fatty acids, cholesterol, white meat and lower intakes of fruits, vegetables, refined grains, low- and high-fat dairy products (Table 2). Individuals in the top tertile of red meat intake had lower intakes of energy, carbohydrates, magnesium, and total dietary fiber compared with those in the lowest tertile. Mean daily intakes of other dietary variables were not different across tertiles of red meat intake.

Biomarkers of glucose metabolism (fasting plasma glucose, serum insulin, HOMA, and QUICKI indexes) across tertile categories of red meat intake are provided in Table 3. High red meat intake was significantly associated with higher fasting plasma glucose and HOMA-IR and lower QUICKI either in the crude or adjusted models, although after additional adjustments for endothelial dysfunction in the last model, these associations disappeared and confirmed our hypothesis that the effect of red meat intake on insulin resistance was mediated through endothelial dysfunction. High red meat intake was significantly associated with higher serum insulin levels (13.9 ± 6.5 versus 6.1 ± 4.1 mU/L) and lower HOMA-B (85 ± 18 versus 120 ± 28) in the crude model. After adjustment for age, energy intake, and other confounding factors,

Table 1. Baseline characteristics of study participants by tertiles of red meat intake[a)]

	Tertiles of energy—adjusted red meat intake			
	T1 ($n = 140$)	T2 ($n = 140$)	T3 ($n = 140$)	p[b)]
Age (years)	35.4 ± 7.1	35.9 ± 7.5	34.2 ± 6.9	0.14
Weight (kg)	62.0 ± 9.4	63.2 ± 9.9	69.8 ± 81.7	0.35
BMI (kg/m^2)	23.5 ± 3.6	24.2 ± 3.5	24.3 ± 3.5	0.14
Waist circumference (cm)	79.3 ± 10.3	82.0 ± 10.0	81.2 ± 10.0	0.09
Systolic blood pressure (mm Hg)	107 ± 13	108 ± 10	109 ± 11	0.79
Diastolic blood pressure (mm Hg)	70 ± 10	69 ± 9	71 ± 9	0.28
Physical activity (MET-h/wk)	79.9 ± 81.1	76.0 ± 79.1	77.7 ± 98.4	0.96
Current OCP use (%)	5.1	5.8	8.8	0.43
Current corticoid steroids use (%)	0.7	1.5	2.2	0.60
Menopausal (%)	6.4	7.2	3.6	0.40
Socioeconomic status[c)] High (%)	40	45	58	0.16
Medium (%)	38	43	31	
Low (%)	22	12	11	
Married (%)	74.1	71.9	73.9	0.90
Overweight or obese[d)] (%)	32.6	42.7	41.7	0.17

a) Data are means ± SD unless indicated.
b) Obtained from analysis of variance for continuous variables and chi-square for categorical variables.
c) High socioeconomic status was defined based on educational level, income, family size, being owner of the house or renting the house, house area, being owner of the car and number and kind of the car(s), number of bedrooms, and determination of who was in charge of the family.
d) BMI ≥25 kg/m^2.

this association remained statistically significant. In model III, red meat intake tended to be associated with increased serum insulin levels. In addition, HOMA-B in the highest tertile of red meat intake tended to be less than lowest tertile, but after adjusting for BMI, the association was no longer significant ($p = 0.07$).

Multivariable-adjusted means of markers of endothelial function across tertile categories of red meat intake are shown in Table 4. Red meat consumption was associated with greater concentrations of E-selectin, sICAM-1, and sVCAM-1. These associations remained significant even after adjusting for potential confounders (E-selectin (73 ± 27 versus 64 ± 21 ng/L), sICAM-1 (238 ± 61 versus 195 ± 71 mg/L) and sVCAM-1 (497 ± 141 versus 407 ± 129 mg/L)). In a sensitivity analysis, when women with corticosteroid use were excluded from the analyses, the results did not alter (data not shown).

4 Discussion

In the present study, high red meat intake was associated with unfavorable plasma concentrations of endothelial function biomarkers and abnormal glucose homeostasis in a sample of Iranian women. These associations remained significant for most outcomes, even after taking potential confounders and dietary variables into account; although after adjustment for BMI, the associations between red meat intake and serum insulin levels and HOMA-B were no longer significant. To our knowledge, this observational study is among the first investigations examining red meat intake in relation to insulin resistance and markers of endothelial function. In addition, this is the first observational study that investigates such a relationship in a Middle Eastern setting.

Endothelial dysfunction and insulin resistance occur early in atherosclerotic development. Cardiovascular diseases are the leading cause of death in Iran [27] as in many developing and developed countries [28]. Therefore, the primary prevention of coronary heart disease is of great importance. Diet influencing endothelial function and insulin resistance may be a mechanism by which dietary quality affects the development of cardiovascular disease. Many studies, in agreement with our findings, emphasized that a diet rich in red and processed meat consumption is an independent contributor to progression of abnormalities in glucose and lipid profile [11–15].

We found a significant association of red meat intake with markers of endothelial function (E-selectin, sVCAM-1, and sICAM-1) even after adjustment for different potential confounding variables. The effect of red meat intake on sVCAM-1 and sICAM-1 has also been reported in a randomized crossover intervention [17], where two diets, differing only in their red meat and oily fish content, were examined. Consumption of red meat diet resulted in a significant increase in sVCAM-1 and sICAM-1 levels among 25 young iron-deficient women. In a prospective study [29], the meat dietary pattern (high intakes of red meat, refined grain, and butter) was positively associated with E-selectin, and sICAM-1, but not with sVCAM-1. In this study, similar to our findings, after further adjustment for BMI, these associations remained significant. In addition, comparing the red meat-enriched diet with the healthy diet, the investigators found significant associations between red meat intake, particularly processed meat,

Table 2. Dietary intakes of study participants by tertiles of red meat intake[a)]

	Tertiles of age and energy—adjusted red meat intake			
	T1 (42–87 g/day, $n = 140$)	T2 (88–135 g/day, $n = 140$)	T3 (136–227 g/day, $n = 140$)	$p^{b)}$
Food groups				
Red meat (g/day)	73 ± 38	103 ± 41	194 ± 83	<0.001
Vegetables (g/day)	377 ± 285	294 ± 174	358 ± 235	<0.001
Fruits (g/day)	474 ± 384	349 ± 280	347 ± 287	<0.001
White meat (g/day)	87 ± 67	80 ± 66	101 ± 64	0.03
Low-fat dairy (g/day)	435 ± 332	316 ± 250	338 ± 295	<0.001
High-fat dairy (g/day)	78 ± 88	58 ± 53	53 ± 37	<0.001
Refined grains (g/day)	463 ± 247	363 ± 233	353 ± 182	<0.001
Whole grains (g/day)	71 ± 102	62 ± 114	53 ± 86	0.31
Nuts and legumes (g/day)	59 ± 43	57 ± 49	64 ± 42	0.41
Nutrients				
Total energy (kcal/day)	3012 ± 956	2458 ± 902	2850 ± 937	<0.001
Protein (g/day)	117 ± 84	115 ± 100	128 ± 158	0.60
Carbohydrate (g/day)	407 ± 151	294 ± 123	294 ± 111	<0.001
Fat (g/day)	108 ± 37	94 ± 37	120 ± 97	<0.001
Saturated fatty acids (g/day)	26 ± 11	24 ± 11	27 ± 17	0.08
MUFA (g/day)	33 ± 12	30 ± 12	48 ± 146	0.16
Poly unsaturated fatty acids (g/day)	41 ± 15	37 ± 15	49 ± 47	<0.001
Cholesterol (mg/day)	243 ± 109	221 ± 121	265 ± 132	0.01
Magnesium (mg/day)	293 ± 117	243 ± 97	273 ± 107	0.01
Iron (mg/day)	24 ± 11	19 ± 8	25 ± 50	0.16
Zinc (mg/day)	9 ± 4	9 ± 5	10 ± 8	0.15
Vitamin B6 (mg/day)	2 ± 0.9	1.7 ± 0.8	2.6 ± 8.3	0.23
Total dietary fiber (g/day)	24 ± 12	18 ± 8	22 ± 19	<0.001

a) All values are means ± SEM.
b) Obtained from ANOVA.

and markers of endothelial function [30, 31]. However, some studies did not reach any significant relations between red meat intake and biomarkers of endothelial dysfunction [32]. Different study design and populations, role of confounding variables, and considering the effect of cooking methods might provide some reasons for discrepant findings.

In the current study, greater red meat intake was associated with insulin resistance and abnormal glucose homeostasis. However, serum insulin levels were not associated with red meat intake after adjusting for BMI. Our findings are consistent with findings of a recent cross-sectional study in which Ley et al. [16] found greater total, unprocessed and processed red meat intakes to be associated with higher fasting insulin and lower adiponectin levels. Similar to our findings, after adjustment for BMI, the association between red meat intake and fasting insulin was substantially attenuated and was no longer significant in their study [16]. Some other studies have reported a significant inverse association between red meat intake and insulin sensitivity [17]. However, others have not reached such findings [18–20]. However, it is noteworthy that different studies have used different indexes to define insulin sensitivity and insulin resistance [16].

Although we were interested in examining the separate associations between processed and unprocessed red meat intake and outcome variables of the current study, low consumption of processed red meat in the study population led us to consider total red meat, rather than processed and unprocessed red meat intake, in relation to dependent variables. Totally, mean consumption of processed red meat in the study population was 8 ± 4 g/day. However, when we considered only unprocessed red meat intake, the findings did not change. Some studies have reported a significant association between unprocessed red meat intake and cardiovascular outcomes [11–16]. Our findings did also reveal that even unprocessed red meat intake might contribute to insulin resistance and endothelial dysfunction. Although unprocessed red meat consumption may have smaller effects on chronic disease, no evidence suggested any cardio-metabolic benefit for unprocessed red meat consumption. Healthier alternatives such as fish, nuts, fruits, whole grains, and vegetables are vastly preferable dietary choices to consuming unprocessed red meat [33].

The potential mechanisms through which red meat consumption might affect endothelial function and insulin resistance are not well understood. Previous studies have shown that increased intake of unprocessed and processed red meat was associated with weight gain [34]. As suggested in some studies, increased adiposity might be the main contributor of the association between red meat intake and insulin resistance [35]. Therefore, it seems that obesity can worsen endothelial dysfunction. But in the present study, the association between intakes of red meat and increased

Table 3. Glycemic variables across tertile categories of red meat intake among participants[a)]

	Tertiles of energy—adjusted red meat intake			
	T1 ($n = 140$)	T2 ($n = 140$)	T3 ($n = 140$)	p for trend[f)]
FPS (mg/dL)				
Crude	78 ± 11	80 ± 12	86 ± 12	0.03
Model I[b)]	77 ± 9	82 ± 11	89 ± 10	0.01
Model II[c)]	79 ± 9	81 ± 10	88 ± 10	0.01
Model III[d)]	81 ± 9	83 ± 10	87 ± 10	0.04
Model IV[e)]	83 ± 8	83 ± 9	85 ± 9	0.22
HOMA-IR				
Crude	1.1 ± 1.6	1.9 ± 1.6	2.4 ± 1.6	0.03
Model I	1.3 ± 1.5	1.9 ± 1.4	2.2 ± 1.6	0.03
Model II	1.5 ± 1.4	1.8 ± 1.3	2.2 ± 1.7	0.04
Model III	1.6 ± 1.5	1.9 ± 1.5	2.0 ± 1.1	0.05
Model IV	1.7 ± 1.4	1.8 ± 1.5	1.8 ± 1.3	0.32
HOMA-B				
Crude	120 ± 28	141 ± 38	85 ± 18	0.02
Model I	117 ± 25	135 ± 36	89 ± 20	0.03
Model II	111 ± 22	137 ± 32	84 ± 21	0.02
Model III	102 ± 25	130 ±3 1	91 ± 20	0.07
Model IV	98 ± 24	124 ± 28	94 ± 22	0.19
QUICKI				
Crude	0.36 ± 0.01	0.28 ± 0.1	0.16 ± 0.02	0.01
Model I	0.36 ± 0.01	0.29 ± 0.1	0.17 ± 0.01	0.01
Model II	0.33 ± 0.01	0.31 ± 0.1	0.16 ± 0.02	0.02
Model III	0.30 ± 0.01	0.32 ± 0.1	0.20 ± 0.02	0.04
Model IV	0.28 ± 0.01	0.30 ± 0.1	0.22 ± 0.02	0.09
INSULIN (mU/L)				
Crude	6.1 ± 4.1	7.6 ± 7.2	13.9 ± 6.5	0.03
Model I	6.5 ± 4.4	8.0 ± 6.7	12.4 ± 6.1	0.04
Model II	6.9 ± 4.2	8.2 ± 7.0	11.9 ± 6.0	0.04
Model III	7.7 ± 3.8	8.0 ± 6.7	10.6 ± 6.1	0.07
Model IV	8.1 ± 3.6	8.2 ± 6.2	10.0 ±5.7	0.11

a) All values are means ± SD.
b) Model I: adjusted for age, energy intake, physical activity (MET-h/wk), current corticoid steroids use (yes or no), current OCP use (yes or no), marital status (categorical), menopausal status (yes or no), systolic blood pressure, diastolic blood pressure, and socioeconomic status (categorical).
c) Model II: Additionally adjusted for intakes of refined and whole grains, fruits, vegetables, white meat, low- and high-fat dairy and percentage of energy from fat, nuts, and legumes.
d) Model III: Further adjusted for BMI.
e) Model IV: Additionally adjusted for markers of endothelial dysfunction.
f) p-Value was calculated from linear regression of glycemic indexes on a categorical variable of red meat intake.
FPS: Fasting plasma glucose.

levels of sICAM-1, sVCAM-1, and E-selectin remained significant even after adjustment for BMI. There are also other proposed underlying mechanisms that may explain how high red meat intake is associated with impaired glucose metabolism and endothelial dysfunction. The saturated fat and cholesterol content of red meat might play a role in its relationship with insulin resistance and endothelial dysfunction [34]. Also, dietary heme iron may increase oxidative stress and insulin resistance, and in some studies has been associated with higher risk of insulin resistance [36]. In addition, some preservatives used in processed meats, such as nitrates and their byproducts (e.g. peroxynitrite), that experimentally promote endothelial dysfunction, atherosclerosis, and insulin resistance [36] may play a role. Furthermore, different meat preparation methods can also provide some explanations for the association between red meat intake and insulin resistance and endothelial function [37].

Our study is suffering from some limitations. The major one is its cross-sectional nature, which would not allow conferring causality. However, the appropriate analysis of cross-sectional data represents a valuable initial step in identifying diet–disease relations. Our findings cannot be extrapolated to the general Iranian population due to its confinement to a selected group of individuals (i.e. female nurses living in Isfahan). Although we controlled for several lifestyle factors associated with red meat intake, residual confounding due to unknown confounding factors cannot be excluded.

In conclusion, we found that high red meat intake is associated with unfavorable plasma concentrations of

Table 4. Indexes of endothelial function across tertile categories of red meat intake among participants[a)]

	Tertiles of energy—adjusted red meat intake			
	T1 ($n = 140$)	T2 ($n = 140$)	T3 ($n = 140$)	p for trend[f)]
E-selectin (ng/L)				
Crude	62 ± 25	48 ± 21	85 ± 31	<0.001
Model I[b)]	60 ± 24	51 ± 23	87 ± 30	<0.001
Model II[c)]	63 ± 22	51 ± 20	81 ± 29	<0.001
Model III[d)]	66 ± 23	55 ± 22	73 ± 28	0.01
Model IV[e)]	64 ± 21	52 ± 21	73 ± 27	0.02
sICAM-1 (mg/L)				
Crude	178 ± 74	228 ± 83	249 ± 66	0.01
Model I	182 ± 71	223 ± 80	241 ± 62	0.01
Model II	185 ±70	220 ± 81	242 ± 61	0.01
Model III	192 ± 72	217 ± 78	235 ± 60	0.03
Model IV	195 ± 71	218 ± 76	238 ± 61	0.03
sVCAM-1 (mg/L)				
Crude	388 ± 137	446 ± 151	510 ± 148	0.01
Model I	381 ± 139	444 ± 148	512 ± 145	0.01
Model II	392 ± 135	449 ± 143	503 ± 141	0.01
Model III	397 ± 132	456 ± 141	508 ± 143	0.01
Model IV	407 ± 129	459 ± 140	497 ± 141	0.02

a) Values are means ± SD in the table and were computed by the use of ANCOVA.
b) Model I: adjusted for age, energy intake, physical activity (MET-h/wk), current corticoid steroids use (yes or no), current OCP use (yes or no), marital status (categorical), menopausal status (yes or no), systolic blood pressure, diastolic blood pressure, and socioeconomic status (categorical).
c) Model II: Additionally adjusted for intakes of refined and whole grains, fruits, vegetables, white meat, low- and high-fat dairy and percentage of energy from fat, nuts, and legumes.
d) Model III: Further adjusted for BMI.
e) Model IV: Further adjusted for blood lipids and glucose.
f) p-Value was calculated from linear regression of adhesion molecules on a categorical variable of red meat intake.

endothelial function biomarkers and abnormal glucose homeostasis among Iranian women. Prospective cohort studies are required to confirm these findings.

FB and AE contributed in conception, design, statistical analysis, and drafting of the manuscript. EF, AHK, PS, and AY contributed in data collection and manuscript drafting. AE supervised the study.

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