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Influence of Diet Behavior on Insulin Resistance in Hypertensive Black Sub-Saharan Africans: A Multicentric, Cross-Sectional Study

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Abstract

Background: Insulin resistance (IR) is the backbone of cardiovascular diseases (CVDs). The later are the most common non-communicable diseases globally. Diet is an important determinant of CVDs. The link between diet and cardiovascular health could be explained by an association between diet pattern and IR. **Aims**: To investigate the association between salt and specific food consumption as well as different diet patterns (Mediterranean, westernized, and intermediate dietary patterns) with HOMAIR as a surrogate marker of IR, and fasting insulin in Black, sub-Saharan essential hypertensive patients. **Methods**: The multicentric, cross-sectional analysis involved 77 Congolese Black hypertensive participants with no history of cardiovascular disease. Daily sodium chloride intake (NaCl g/24h) was estimated from 24-hour urine collection. Dietary behaviours were evaluated through a semi-quantitative food frequency questionnaire (FFQ). Homeostatic model assessment of insulin resistance (HOMAIR) ≥ 2.5 was used as surrogate marker of IR. **Results**: A decrease in weekly consumption of fruits, vegetables and fish would significantly explain an increase of 29% ($r = 0.292$; $p = 0.010$), 24% ($r = 0.242$; $p = 0.034$) and 23% ($r = 0.226$; $p = 0.048$) of the value of HOMAIR respectively. In contrast, an increase in daily sodium chloride intake was associated with 28% ($r = 0.283$, $p = 0.027$) of the increase in HOMAIR. Also, a decrease in the average weekly consumption of fruit, vegetables and fish would significantly explain an increase of 25% ($r = 0.247$; $p = 0.030$), 30% ($r = 0.302$; $p = 0.008$) and 31% ($r = 0.313$; $p = 0.006$) of fasting insulin. In contrast, an increase in red meat consumption was associated with a 26% increase ($r = 0.257$, $p = 0.024$) in fasting insulin. In multivariable adjusted analysis 45% of variation in fasting insulin ($R^2 = 0.452$; overall $p = 0.005$) were explained by fruits, vegetables and fish consumption. 38% of variation in HOMAIR ($R^2 = 0.379$; overall $p = 0.047$) were explained by fruits and vegetable consumption and daily sodium chloride intake (NaCl g/24h). **Conclusions:** In hypertensive Black sub-Saharan Africans, Salt intake and westernized diet seem to promote insulin resistance whereas Mediterranean diet, fruits, vegetables and fish consumption enhance insulin sensitivity.

Keywords

Diet Behavior, Insulin Resistance, Hypertension, Black, Sub-Saharan Africans

1. Introduction

Cardiovascular diseases (CVDs) are a real scourge of our time, responsible for an estimated 17.8 million deaths in 2017, of which more than three quarters were in low-income and middle-income countries [1].

Globalization, and the cohort of changes it is making in the way of life for people nowadays, is the main cause of the ongoing outbreak of CVDs in all regions of the world. Among these changes, dietary behavior is among the most obvious, especially in sub-Saharan Africa (SSA), where rapid and ongoing food system transformations have been noted [2] [3] [4] [5]. For many authors, this nutritional transition could explain, at least in part, the emergence of CVDs in this part of the globe [5] [6].

Diet is a key determinant of CVD, and dietary modification has been shown to significantly decrease the risk of coronary heart disease (CHD) by attenuating related risk factors such as hypertension (HTN), hyperglycemia, elevated low-density lipoprotein cholesterol (LDL-C) level, oxidative stress, and inflammation [7]-[12].

HTN is a major contributor to global mortality and incapacity [13]. In sub-Saharan Africa, HTN affects younger people, is poorly controlled and often leads to target organ damage at an earlier age and with more severe cardiovascular complications [14]. Hypertensive patients with insulin resistance (IR) are at increased risk of cardiovascular events compared to hypertensive patients without IR [15].

On the other hand, Insulin resistance (IR) plays a central role in the pathogenesis and progression of CVDs [16] [17] [18]. Alongside cardiovascular disease, its prevalence increases with an epidemic scale, as a result of an ongoing epidemiological transition in populations lifestyle inherent in globalization [19] [20] [21]. Furthermore, the results of various studies suggest a link between diet and insulin resistance both in humans [22] [23] [24] [25] [26] and in laboratory animals [27] [28] [29]. The link between diet and CVDs could be explained, at least in part, by an association between diet pattern and IR. Thereby, the best preventive approach to cardiovascular disease would likely be to fight IR. Dietary measures should be the spearhead of this fight. Numerous works and even meta-analyzes exist on the associations between different foods consumption and the development of insulin resistance. Most are weak in ignoring confounding factors such as body mass index, waist circumference and sedentary time (ST), while these factors have been shown to be linked to insulin resistance. Moreover, almost none of these studies have been conducted on a hypertensive black sub-Saharans. To fill this information gap, this study aims to investigate the association between salt and specific food consumption as well as different diet patterns (Mediterranean, westernized, and intermediate dietary patterns) with HOMAIR and fasting insulin in sub-Saharan essential hypertensives, while minimizing the methodological weaknesses of previous studies that have been conducted elsewhere.

2. Materials and Methods

The present cross-sectional multicentric analysis used data from 77 hypertensive participants with no history of CVD. The participants were consecutively selected during outpatient consultations in 5 hospitals in Kinshasa, capital of the Democratic Republic of Congo, for 5 consecutive days during the so-called "Heart Week", from Tuesday September 24, 2019, World Heart Day, to Saturday September 28, 2019. The hospitals involved have the distinction of possessing an individualized cardiology unit. These are the University Hospital of Kinshasa, the General Provincial Reference Hospital of Kinshasa, the Centre Médical de Kinshasa (CMK), the Lomo-Médical Clinic, and the Ngaliema Clinic.

Participants underwent a complete assessment of socio-demographic (*i.e.*, age, sex), dietary, body measurements, sedentary and glucoregulation parameters (fasting blood glucose, glycated hemoglobin (HbA1c) and fasting insulinemia. Socio–demographic, sedentary and dietary characteristics were collected by trained interviewers using a standardized questionnaire in each of the 5 aforementioned recruitment hospitals during the Heart Week. Body measurements and glucoregulation parameters were taken at the CMK during an individual appointment during the 2-week period following recruitment. The CMK is a reference clinic, working to international standards and norms, with, among other things, an accredited clinical biology laboratory and a special unit named the "*pôle de cardiologie*" ("cardiology center") with highly qualified and regularly retrained personnel that conducts cardiovascular explorations such as Doppler echocardiography, coronary scanning, and cardiopulmonary exercise testing. A cardiovascular rehabilitation unit, the only one in central Africa, also operates there.

2.1. Patient Selection

Consecutive asymptomatic patients with presumed essential hypertension attending the outpatient clinic at 5 aforementioned recruitment hospitals during Heart Week 2019 were the target of this study. They were screened for clinical or laboratory evidence of secondary hypertension, renal disease, and hepatic disease.

The inclusion criteria were age of 20 years and above, and absence of clinical or laboratory evidence of secondary hypertension, renal disease, or hepatic disease. Patients with heart disease unrelated to high blood pressure, as well as those using diuretics, were excluded from participation. Hypertensives meeting the inclusion criteria were invited in writing to participate in the present study, for which they gave written informed consent.

2.2. Study Procedures

Anamnestic data

Demographic data (age, sex), lifestyle habits (heavy alcohol consumption, current smoking, sedentary and dietary behavior), medical history including cardiovascular risk factors (age at diagnosis of high blood pressure, history of diabetes mellitus, dyslipidemia, hyperuricemia, menopause) and previous cardiovascular events (stroke, ischemic heart disease, heart failure, chronic kidney disease, cardiovascular surgery), and current medication use for chronic disease (antihypertensive treatment, anti-diabetic treatment, and other treatments including statins, antiplatelet agents, hypouricemics, oral contraception, hormone replacement therapy) were collected during an in-person, directed interview using an ad-hoc questionnaire. Sedentary behavior was assessed using the World Health Organization's Global Physical Activity Questionnaire (WHO/GPAQ) [30]. Dietary behaviors were evaluated through a semi-quantitative food frequency questionnaire (FFQ) [31]. The foods on which the participants were asked about their frequency of consumption are the following: fruits, vegetables, nuts, legumes (soybeans, beans, peas, peanuts), fish, cereals (corn, wheat, rice, sorghum), dairy products, red meat. For each specific food item, the participant was asked for their average weekly intake frequency of a standard portion size.

Anthropometric data

Anthropometric parameters, measured by a trained observer, consisted of measurements of body weight, height, waist and hip circumference according to WHO recommendations. Body weight was measured in kilograms, to the nearest 100 g, using a validated electronic balance on a stable, flat surface, with the participant wearing light clothing and shoes. Height was measured to the nearest centimeter, using a measuring rod, with participants standing barefoot and bareheaded. Waist circumference was measured to the nearest millimeter using a measuring tape applied directly to the skin along the horizontal line passing through the umbilicus. Body mass index (BMI) was calculated as BMI = Body weight (kg) ÷ height (m)^2. The body surface area (BSA) was calculated using the DuBois formula [14] as follows:

$$\text{BSA} = \text{height (cm)}^{0.725} \times \text{weight (kg)}^{0.425} \times 0.007184.$$

Blood pressure

BP was measured non-invasively by 24 hour-ambulatory blood pressure monitoring (ABPM) using a TONOPORT V (GE Health care, Freiburg, GERMANY) recorder. During this recording, participants were asked to maintain their usual living habits.

2.3. Laboratory Measurements

Glucoregulation parameters

For all analyzes, a blood sample was taken between 7 a.m. and 9 a.m. from the cubital vein of the patient fasting since 10 p.m. of the previous day. All analyzes were carried out at the CMK laboratory. The blood glucose test was performed on plasma oxalate by colorimetric method using standard reagents (Biolabo) and measured by the HELIOS Epsilon spectrophotometer. The dosage of insulin was performed on EDTA plasma by ELISA. Reading the optical density was done on a string read from the firm HUMAREADER HUMAN (Germany). The HOMAIR was calculated as HOMAIR = fasting insulin (μU/ml) × fasting glucose (mmol/l)/22.5 [32]. The determination of HbA1c was performed by the immunoturbidimetric technique using the biochemistry analyzer COBAS C111.

Daily sodium chloride intake

Each participant was given a urine collection kit, comprising a urine container with an integrated unit for closed urine transfer using the V-Monovette® (Nümbrecht, Germany) vacuum system. Instruction for use was provided orally and in writing. Participants were instructed to discard the first morning void but to collect all voids throughout the rest of the day until and including the morning void of the day after. The container was to be kept cool throughout collection. Urine collection containers were returned to the medical laboratory of the CMK, where contents were mixed, and the total volume was recorded. Then, 2 mL samples of each participant's urine were extracted and stored at −20˚C. Urinary sodium levels were assessed using a Roche Hitachi (Indianapolis, IN, USA), indirect ion-selective electrode to determine ion concentration.

Estimated daily sodium chloride intake (NaCl g/24h) was calculated from sodium excretion using Formula [33]:

$$\text{NaCl (g/24h)} = \text{Na (mmol/24 h)} \times 58.4/1000$$

2.4. Operational Definitions

Lifestyle data

Cigarette smoking was defined as regular smoking for at least 30 days preceding the interview date, regardless of the number of cigarettes smoked [34].

Heavy alcohol consumption was defined as drinking more than 2 glasses of beer or its equivalent every day for at least a year [35].

Moderate red wine consumption was defined as a daily red wine intake not exceeding 1 large glass (250 ml), or approximately 30 g of alcohol [36].

Sedentary defined as sitting more than 7 hours daily [37].

High consumption of a specific food was defined as being consumed, on average, 4 to 7 days per week.

Low consumption of a specific food has been defined as an average weekly consumption frequency of fewer than 4 times per week.

Excessive sodium intake has been defined as greater than or equal to 5 g of dietary sodium per day [38].

The Mediterranean diet has been defined as comprising a high amounts consumption of at least four of the followings: fruits, vegetables, nuts, legumes (including soybeans, beans, peas, peanuts), fish, cereals (including corn, wheat, rice, sorghum); moderate intake of red wine and low amounts of dairy products and red meat.

The westernized diet has been defined as comprising a high consumption of red meat and dairy products and a low consumption of at least four of the followings: fruits, vegetables, nuts, legumes (including soybeans, beans, peas, peanuts), fish, cereals (including corn, wheat, rice, sorghum [39]).

Participants who did not meet the criteria of the two previous diet patterns were classified in an intermediate pattern (Idp).

Anthropometric parameters

Overweight was defined as a BMI between 25 and 29.9 kg/m^2 of body surface area [40].

Obesity was defined as a BMI equal to or greater than 30 kg/m^2 of body surface area [40]. Abdominal obesity was defined as a waist circumference exceeding 102 cm and 88 cm for men and women, respectively [40].

Bioclinical data

Poor control of arterial hypertension was defined as an average systolic blood pressure greater than 130 mm Hg and/or average diastolic BP greater than 80 mm Hg on 24-hour ambulatory blood pressure monitoring [41].

Laboratory Parameters

Hyperinsulinemia was defined as fasting insulin > 90 pmol/l [42].

Insulin resistance was defined by a HOMAIR ≥ 2.5 [43].

2.5. Statistical Analysis

Data are presented as number (n) and relative frequencies (%) for categorical variables and average (±standard deviation) for quantitative variables. Paired comparisons were carried out by Pearson Chi-square or Fischer's Exact test as appropriate for categorical variables and multiple comparison of continuous variables (means and medians) by ANOVA and H test of Kruskal Wallis. ANOVA tests found to be significant at the threshold of $p < 0.05$ were supplemented by a post hoc test by Scheffé. The influence of specific foods item on HOMAIR and insulinemia was investigated by linear regression in simple exploratory analysis. Correlation coefficients (r) were calculated to determine the degree of association between specific food items and dietary patterns on the one hand and insulinemia and HOMAIR on the other. When differences were observed between foods items consumption frequency and HOMAIR or insulinemia, the effect of potential confounders was studied by adjustment in multiple linear regression. Finally, the determination coefficients (R^2), were calculated to determine the degree of association between foods items consumption and HOMAIR or insulin. The significance threshold was $p < 0.05$. Statistical analyzes were performed using XLStat 2020 (Oxford, UK) and SPSS (Statistic Package for Social Sciences) 20 for Windows version 24 software (Chicago, USA).

2.6. Ethical Considerations

This research was conducted in strict compliance with the recommendations of the Helsinki Declaration III. Approval to conduct the study was obtained from the ethics committee of the University of Kinshasa Public Health School prior to its commencement. Each participant provided written informed consent to participate in the study. All respondents were debriefed on the results of the study.

3. Results

A total of 77 hypertensive participants were included in the final analysis based on availability of the analyzed data. Mean age of the study population was 48.7 ± 10.4 years with 52% of men (sex ratio 1M/1F). Table 1 reports that the NaCl g/24h and the average weekly fruit, vegetables, meat, fish consumption and the different diet patterns did not seem to differ between men and women ($p > 0.05$). Furthermore, men had a wider WC and higher average HbA1C than women (6.1 ± 0.8 vs 5.6 ± 1.0; $p = 0.021$).

In Table 2, it can be seen that the mean values of WC ($p = 0.006$), insulin ($p = 0.040$) and HOMAIR ($p = 0.042$) increase significantly with increasing age. The frequency of IR is significantly higher in participants over 50 years of age ($p = 0.007$). When considering specific foods, there is no difference in the average consumption frequency between different age groups. However, when considering the diets patterns, it is noted that the frequency of the Mdp decreases significantly with increasing age; on the other hand, that of the Wdp increases significantly with increasing age.

Relationship between Insulin with Diet pattern and Salt intake

Figure 1 shows that participants on the Wdp had significantly higher mean insulin values compared to those on the Mdp ($p = 0.004$) and Idp ($p = 0.013$). in contrast, the insulin averages of participants on the Mdp and Idp were not different ($p = 0.995$).

As shown in Figure 2, the mean insulin value of participants with excessive salt intake appears to be higher than that of participants on normal salt intake, but the difference was not statistically significant ($p = 0.098$).

Relationship between HOMAIR with diet patterns and salt intake

Figure 3 shows that participants on a Wdp have significantly higher mean values of HOMAIR compared to those on a Mdp ($p < 0.001$) and Idp ($p = 0.007$). On the other hand, the HOMAIR averages for patients on the Mdp and Idp were not different ($p = 0.845$).

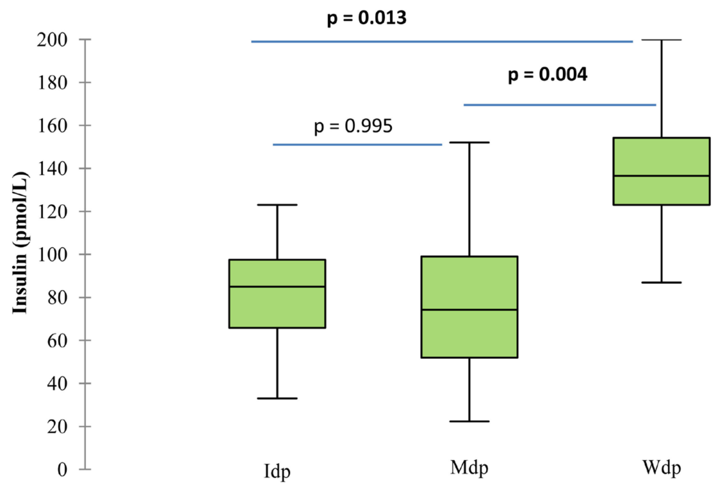

Figure 1. Average insulin values versus diet pattern.

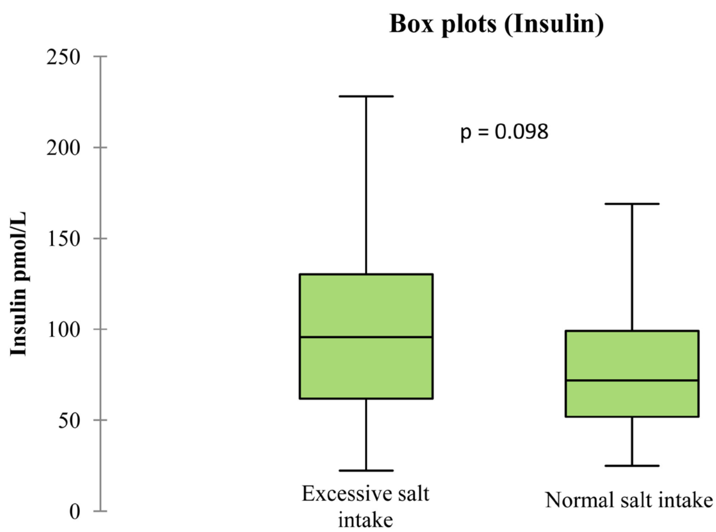

Figure 2. Average insulin values in relation to salt intake.

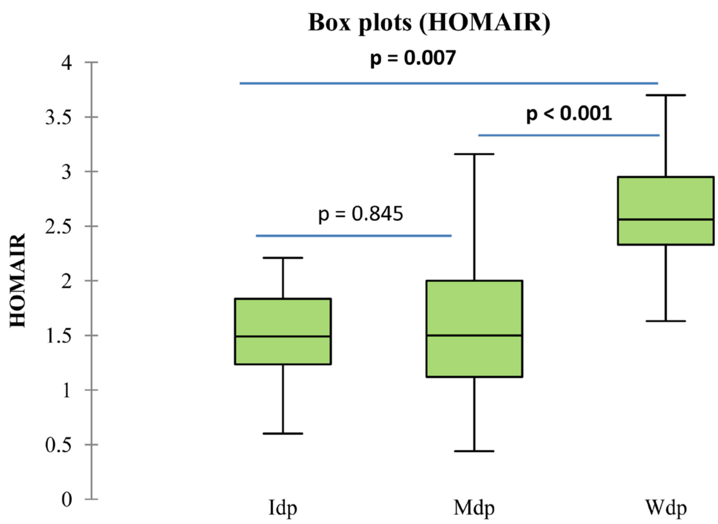

Figure 3. Average values of the HOMAIR according to the type of diet.

Table 1. General characteristics of study participants.

Variables	All n = 77	Male n = 40	Female n = 37	p-value
Age (years)	48.7 ± 10.4	50.2 ± 9.7	47.1 ± 10.9	0.189
Age groups (years)				0.139
≤40	21 (27.3)	7 (17.5)	14 (37.8)	
41 - 50	27 (35.1)	16 (40.0)	11 (29.7)	
>50	29 (37.7)	17 (42.5)	12 (32.4)	
BMI (kg/m^2)	30.5 ± 4.7	30.7 ± 4.6	30.3 ± 4.7	0.672
WC (Cm)	102.9 ± 12.1	107.3 ± 13.6	98.7 ± 8.7	**0.004**
ST (hour/day)	9.4 ± 2.4	9.1 ± 2.2	9.8 ± 2.6	0.217
Insulin (pmol/l)	95.8 ± 48.5	93.2 ± 48.8	98.5 ± 48.7	0.634
HOMAIR	1.9 ± 0.9	1.8 ± 0.9	2.0 ± 1.0	0.439
Glycemia (mmol/L)	5.5 ± 1.6	5.7 ± 1.6	5.2 ± 1.6	0.187
HbA1C (%)	5.8 ± 0.9	6.1 ± 0.8	5.6 ± 1.0	**0.021**
Diet (days per week)				
Fruits	3.0 ± 1.8	3.0 ± 1.8	4.0 ± 1.8	0.163
Vegetables	5.0 ± 1.5	5.0 ± 1.5	5.0 ± 1.6	0.694
Legumes	4.0 ± 1.4	4.0 ± 1.2	4.0 ± 1.8	0.652
Cereals	5.0 ± 1.2	5.0 ± 1.4	5.0 ± 1.6	0.451
Nuts	2.0 ± 1.1	2.0 ± 1.5	2.0 ± 1.8	0.155
Fish	4.0 ± 1.5	4.0 ± 1.6	4.0 ± 1.4	0.250
Red meat	3.0 ± 1.4	4.0 ± 1.4	3.0 ± 1.5	0.311
Dairy products	2.0 ± 1.1	2.0 ± 1.2	2.0 ± 1.6	0.126
NaCl g/24h	12.0 ± 8.3	12.9 ± 8.0	11.1 ± 8.6	0.329
Insulin resistance	18 (23.4)	8 (20.0)	10 (27.0)	0.592
Diet patterns				0.327
Mdp	37 (48.1)	16 (40.0)	21 (56.8)	
Wdp	21 (27.3)	13 (32.5)	8 (21.6)	
Idp	19 (24.7)	11 (27.5)	8 (21.6)	
Salt intake				0.328
Normal	21 (27.3)	9 (22.5)	12 (32.4)	
Excessive	56 (72.7)	31 (77.5)	25 (67.6)	

BMI = Body Mass Index; WC = Waist Circumference; ST: Sedentary Time; HOMAIR = Homeostatic Model Assessment for Insulin Resistance; HbA1C = glycated hemoglobin; NaCl g/24h = Estimated daily sodium chloride intake; Mdp = mediterranean diet pattern; Wdp = westernized diet pattern; Idp = intermediate diet pattern.

Figure 4 illustrates that the mean HOMAIR value of participants with excessive salt intake was high compared to that of participants on normal salt intake with a statistically significant difference (p = 0.024).

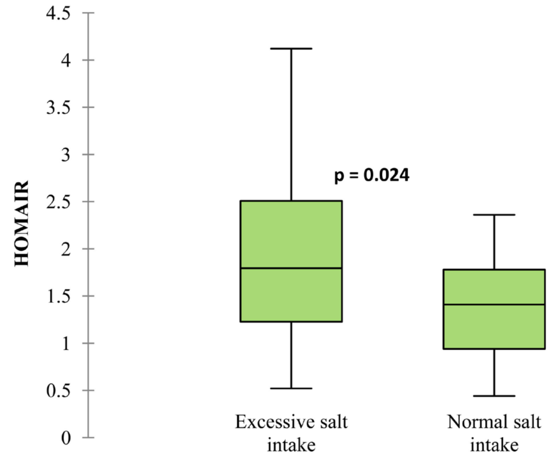

Figure 4. Average values of HOMAIR according to salt intake.

Table 2. General characteristics of study participants according to age group.

Variables	≤40 years n = 21	41 - 50 years n = 27	>50 years n = 29	p
BMI (Kg/m^2)	28.8 ± 5.2	30.8 ± 4.2	31.4 ± 4.5	0.145
WC (cm)	96.1 ± 11.0	103.0 ± 8.9	107.9 ± 13.2	**0.006**
ST (hour/day)	9.0 ± 2.7	9.9 ± 2.4	9.3 ± 2.1	0.445
Insulin (pmol/L)	81.0 ± 48.7	88.4 ± 48.5	113.3 ± 44.5	**0.040**
HOMAIR	1.5 ± 0.9	1.9 ± 1.1	2.1 ± 0.9	**0.042**
HbA1C (%)	6.1 ± 1.4	5.6 ± 0.7	5.8 ± 0.8	0.300
Glycemia (mmol/L)	5.7 ± 2.1	5.3 ± 1.2	5.5 ± 1.5	0.760
Diet (average weekly consumption)				
Fruits	3.1 ± 1.7	3.3 ± 1.9	3.3 ± 1.7	0.888
Vegetables	4.8 ± 1.4	4.6 ± 1.8	4.5 ± 1.4	0.772
Legumes	5.2 ± 1.3	5 ± 1.5	4 ± 1.4	0.615
Cereals	5.6 ± 1.2	5 ± 1.6	4 ± 1.0	0.453
Nuts	4.5 ± 1.4	5 ± 1.7	3 ± 1.6	0.845
Fish	3.9 ± 1.3	3.9 ± 1.8	3.6 ± 1.4	0.656
Red meat	2.9 ± 0.9	3.3 ± 1.7	3.8 ± 1.3	0.058
Dairy products	2.8 ± 0.1	2.1 ± 1.8	2.3 ± 1.9	0.089
NaCl g/24h	13.6 ± 2.9	12.1 ± 5.8	10.8 ± 5.7	0.491
Insulin resistance	3 (14.3)	4 (14.8)	11 (37.9)	**0.044**
Diet patterns				**0.007**
Mdp	14 (66.7)	15 (55.6)	8 (27.6)	
Wdp	5 (23.3)	5 (18.5)	11 (37.9)	
Idp	2 (9.5)	7 (25.9)	10 (34.5)	
Salt intake				0.159
Normal	8 (38.1)	4 (14.8)	9 (31.0)	
Excessive	13 (61.9)	23 (85.2)	20 (69.0)	

BMI = Body Mass Index; WC = Waist Circumference; ST: Sedentary Time; HOMAIR = Homeostatic Model Assessment for Insulin Resistance; HbA1C = glycated hemoglobin; NaCl g/24h = Estimated daily sodium chloride intake; Mdp = mediterranean diet pattern; Wdp = westernized diet pattern; Idp = intermediate diet pattern.

Table 3 shows that an increase in BMI and WC as well as a decrease in average weekly fruit, vegetables and fish consumption significantly explained an increase of48% (r = 0.482; p < 0.001), 32% (r = 0.320; p = 0.001), 29% (r = 0.292; p = 0.010), 24% (r = 0.242; p = 0.034) and 23% (r = 0.226; p = 0.048) of the value of the HOMAIR respectively. On the other hand, an increase in salt intake was associated with 28% (r = 0.283, p = 0.027) of the increase of HOMAIR.

Just as an increase in BMI and WC as well as a decrease in the average weekly fruits, vegetables and fish consumption significantly explained a respective increase of 46% (r = 0.465; p = 0.001), 39% (r = 0.389; p = 0.001), 25% (r = 0.247; p = 0.030), 30% (r = 0.302; p = 0.008) and 31% (r = 0.313; p = 0.006) of insulin value. In contrast, an increase in red meat consumption was associated with 26% (r = 0.257, p = 0.024) increase of fasting insulin.

In a multiple linear regression analysis (**Table 4**) fruits, vegetables and fish consumption emerged as independent determinants of insulin, explaining 45% of its variability.

Table 3. Dietary risk factors associated with fasting insulin and insulin resistance (HOMAIR).

Variables	HOMAIR		Insulin	
	β	r (p-value)	β	r (p-value)
BMI (Kg/m²)	0.10	0.482 (**<0.001**)	4.84	0.465 (**<0.001**)
WC (cm)	0.03	0.320 (**0.010**)	1.66	0.389 (**0.001**)
ST (hour/day)	0.02	0.038 (0.772)	0.10	0.050 (0.968)
Fruits	−0.16	0.292 (**0.010**)	−6.762	0.247 (**0.030**)
Vegetables	−0.16	0.242 (**0.034**)	−9.716	0.302 (**0.008**)
Red meat	0.11	0.162 (0.159)	8.694	0.257 (**0.024**)
Fish	−0.15	0.226 (**0.048**)	−10.018	0.313 (**0.006**)
NaCl g/24h	0.01	0.283 (**0.027**)	0.676	0.116 (0.317)

BMI = Body Mass Index; WC = Waist Circumference; ST: Sedentary Time; HOMAIR = Homeostatic Model Assessment for Insulin Resistance; NaCl g/24h = Estimated daily sodium chloride intake.

Table 4. Dietary independent determinants of fasting insulin.

Variables	Insulin vs diet			Insulin vs diet ajusted for BMI, WC and ST		
	β	ES	p	β	ES	p
(Constante)	135.484	28.383	**0.000**	235.484	38.383	**0.000**
Fruits (days/week)	−3.367	3.132	**0.028**	−2.367	3.258	**0.012**
Vegetables (days/week)	−6.22	3.729	**0.010**	−7.220	3.791	**0.011**
Red meat (days/week)	4.60	3.904	0.243	5.600	3.918	0.243
Fish (days/week)	−6.683	3.784	**0.002**	−3.683	4.784	**0.001**
NaCl g/24h	0.789	0.634	0.217	0.389	0.734	0.217
BMI (Kg/m²)	-	-		4.150	1.591	**0.012**
WC (cm)	-	-		0.403	0.653	**0.045**
ST (hour/day)	-	-		2.400	2.638	0.367
	$R^2 = 0.452$			$R^2 = 0.641$		
Overall p-value	**0.004**			**0.001**		

BMI = Body Mass Index; WC = Waist Circumference; ST: Sedentary Time; HOMAIR = Homeostatic Model Assessment for Insulin Resistance; NaCl g/24h = Estimated daily sodium chloride intake, BMI = Body Mass Index, WC = Waist circumference, ST (Sedentary Time).

As shown in Table 5, after adjusting for confunding factors, fruits consumption, vegetables consumption and NaCl g/24h emerged as independent determinants of HOMAIR, explaining 38% of its variability.

As illustrated in Table 6, after adjusting for confunding factors, total (but non central) obesity, low fruit, vegetable and fish consumption have emerged as independent determinants of Insulin resistance.

Table 5. Dietary independent determinants of HOMAIR.

Variables	HOMAIR/diet			HOMAIR/diet adjusted for BMI, WC and ST		
	β	ES	p	β	ES	p
(Constante)	2.728	0.594	**0.000**	−0.483	1.33	0.761
Fruits	−0.118	0.066	**0.007**	−0.018	0.087	**0.001**
Vegetables	−0.082	0.078	**0.029**	−0.032	0.090	**0.012**
Red meat	0.044	0.082	0.589	−0.040	0.099	0.589
Fish	−0.096	0.079	0.230	−0.145	0.090	0.230
NaCl g/24h	0.009	0.013	**0.003**	0.010	0.016	**0.011**
BMI (Kg/m^2)	-	-	**-**	0.102	0.034	**0.004**
WC (cm)	-	-	**-**	0.001	0.014	**0.019**
ST (hour/day)	-	-	-	0.011	0.056	0.841
	$R^2 = 0.378$			$R^2 = 0.553$		
Overall p-value	**0.047**			**0.007**		

HOMAIR = Homeostatic Model Assessment for Insulin Resistance; BMI = Body Mass Index; WC = Waist Circumference; ST: Sedentary Time; NaCl g/24h = Estimated daily sodium chloride intake, BMI = Body Mass Index, WC = Waist circumference, ST (Sedentary Time).

Table 6. Dietary independent determinants of insulin resistance.

Variables	Univariate analysis		Multiivariate analysis	
	p	OR (95%CI)	p	ORa (95% CI)
Total obesity				
No		1		1
Yes	**0.005**	7.15 (2.52 - 16.14)	**0.035**	2.59 (1.23 - 5.27)
Abdominal obesity				
No		1		1
Yes	**0.012**	5.00 (1.83 - 12.27)	0.215	1.53 (0.34 - 2.70)
Fruit consumption				
Normal		1		1
Low	**0.026**	5.88 (1.48 - 9.38)	**0.011**	3.84 (1.47 - 6.95)
Vegetable consumption				
Normal		1		1
Low	**0.047**	3.13 (1.02 - 9.65)	**0.026**	2.64 (1.51 - 6.33)
Red meat consumption				
Excessive		1		1
Normal	**0.006**	0.20 (0.07 - 0.63)	0.727	0.76 (0.16 - 3.56)
Fish consumption				
Normal		1		1
low	**0.008**	4.56 (1.47 - 14.04)	**0.017**	2.91 (1.64 - 4.93)

4. Discussion

The purpose of the present study was to investigate the associations between salt and specific food consumption as well as different diet patterns (Mediterranean, westernized, and intermediate) with HOMAIR as a surrogate marker of IR, and fasting insulin in Black, sub-Saharan essential hypertensives.

The results of the present study suggest that fruits, vegetables and fish consumption are independent determinants of fasting insulin, explaining 45% of its variability. Similarly, fruits and vegetables consumption as well as the daily sodium chloride intake are independent determinants of HOMAIR, explaining 47% of its variability.

There was a positive and significant correlation between NaCl g/24h and HOMAIR. There was also a positive and significant relationship between red meat consumption and fasting insulin. Inversely, there was à negative and significant relationship between fruits, vegetables and fish consumption not only with insulin but also with HOMAIR.

Gender, age and diet appeared to play a role in the participants' glucoregulation parameters. Thereby, men had a higher average HbA1C than women; the oldest participants seemed to have higher fasting insulin and HOMAIR, and were more often insulin resistant; the younger participants more often had a Mdp while the older more often had a Wdp; participants on the Wdp had significantly higher mean insulin and HOMAIR values compared to those on the Mdp; participants with excessive salt intake had higher HOMAIR values compared to that of participants on normal salt intake.

There are endless foods and many types of diets across the globe and in every population. The foods investigated in this study are found in almost every gastronomy in the world. The varying proportions in which these foods combine in various gastronomies give rise to specific diets patterns. It is classic to dichotomize these diverse diet patterns into two main essential groups: 1) unhealthy ones, proportionally richer in fat and animal foods and of which the westernized diet is the leader, 2) healthy ones, proportionally richer in plant foods of which the Mediterranean diet is the leader. Mediterranean and westernized diet are undoubtedly the most widely described and evaluated dietary patterns in scientific literature. Salt is almost ubiquitous in the gastronomy of the peoples of the planet, and has also been the focus of many studies.

The positive association found in this study between dietary sodium intake and HOMAIR is consistent with the results of previous studies. In a recent Korean study, Park *et al.* found that high sodium intake was correlated with higher plasma insulin levels and increased insulin resistance [44]. Ogihara *et al*., in an experimental study in rats, found that a diet high in salt could be a factor promoting insulin resistance [45]. The following pathophysiological mechanisms could explain this correlation: low sodium consumption lowers blood leptin levels, which leads to a reduction in the size of abdominal fat cells, leading to a decrease in obesity and insulin resistance [46]. Conversely, a high sodium intake would lead to an increase in the blood level of leptin [47] and therefore an increase in insulin resistance. In addition, a low sodium diet regulates the expression of the type 4 glucose transporter (GLUT4), the insulin receptors in fat cells, resulting in a decrease in insulin resistance. [48]. Other studies, however, have found an inverse association between dietary sodium intake and insulin resistance. In a recent 7-week experimental study, Yoshiichi *et al.* demonstrated that high salt intake improved insulin sensitivity, and attributed this improvement to increased plasma levels of adiponectin [47]. Other previous studies, also conducted during short period, have come to a similar conclusion, demonstrating significant association of low-salt diet with higher homeostasis model assessment index [49]. Interestingly, there are also strong pathophysiological arguments to explain these results. Indeed, a high salt intake would lead, by a down-regulation of genes involved in lipogenesis and an up-regulation of genes involved in lipolysis, a decrease in fat mass and in the percentage of abdominal fat. [50]. In addition, a low sodium diet causes a decrease in extracellular volume, which stimulates the renin-angiotensin aldosterone system. High levels of angiotensin II affect the action of insulin [51]. The study of Lima *et al.*, allows us to see an explanation for these divergent, yet pathophysiologically consistent results. In fact, they demonstrated that the improvement in insulin sensitivity induced by a high-salt diet was only transient, and did not persist beyond a certain time [52]. In that study, the higher insulin sensitivity found in the beginning of the survey did not persist after 13 weeks of follow up. Indeed, insulin resistance is a chronic situation that is mainly affected by long-term eating habits. Results observed after short intervention periods could not therefore reflect the reality of chronic exposure. In addition, the different profiles of the populations studied could also explain the differences observed. Finally, the absence of a standardized universal definition of a diet "rich in sodium" or "low in sodium" deserves to be mentioned.

The present study found that an increase in red meat consumption was associated with increase of fasting insulin. Many previous studies, and even meta-analyzes, have reported positive associations between consumption of red meat and insulin resistance [53]-[58]. This association was observed for both unprocessed and processed red meat [58]. Studies on the association between red meat consumption and insulinemia are more rare. In a randomized, crossover acute meal study, Kim *et al.* observed an increase of plasma insulin in response to red meat diet [59]. These same authors observed that the increase in insulinemia in response to a diet rich in red meat was twice that of C-peptide, which suggests a decrease in the clearance of insulin as the underlying mechanism of this hyperinsulinemia. Another explanation is the increase in plasma branched-chain amino acids (BCAAs) induced by red meat rich diet. Indeed, it has been shown that high concentrations of plasma BCAAs cause hyperinsulinemia by stimulating insulin secretion [60] [61] [62].

In the present study, a decrease in average weekly fruit, vegetables and fish consumption significantly explained an increase of the values of the fasting insulin and HOMAIR. This finding is in line with several previous studies. Fernström *et al.* found an inverse association between HOMAIR and fish, fruit and vegetables intake in Swedish young adults [63]. In a large study conducted in 18 countries around the world, the benefit of consuming fruits and vegetables in relation to insulin resistance was underlined [64]. A prospective Chinese study also showed the benefit of fruit consumption on type 2 diabetes [65]. Similarly, more recently, Abbot *et al.* found that DHA-enriched fish oil reduces insulin resistance [66]. Vegetables contain ingredients with antioxidant properties such as phenolic compounds and other vitamins and nutrients [67]. Fruits provide, among many other nutrients, dietary fibre and vitamin C but also flavonoids and terpenes. These nutrients have aintiinflammatoty properties [68] [69] [70] [71]. Fish contain bioactive nutrients such as n-3 long-chain PUFAs eicosapentaenoic acid (EPA) and docosahexaenoic that have anti-inflammatory properties [72] [73]. A growing body of evidence suggests that inflammation and oxidative stress play an important role in the genesis of hyperinsulinemia [74] [75] and insulin resistance [76] [77] [78] [79] [80]. A diet low in fruits, vegetables and fish would therefore deprive the body of an important anti-inflammatory and anti-oxidative defense, and thereby predispose to hyperinsulinemia and insulin resistance.

Men participants of the present study had a higher average HbA1C than women. This is in accordance with the founding of QINGLIN MA and al, who, in a cross-sectional study of 18,265 non-diabetic Chinese participants, had also found that the overall levels of HbA1c were higher in male than that in female [81]. Lower hemoglobin levels are found in adult female animals in many species of mammals, birds and reptiles [82], suggesting that it is an important physiological phenomenon. This would be due to both hormonal factors [82] but also to menstrual cycles. These menstrual cycles result in a faster erythrocyte turnover that would lead to lower glycated hemoglobin levels in women.

The oldest participants seemed to have higher fasting insulin and HOMAIR, and were more often insulin resistant. Many previous studies have examined the effects of aging on insulinemia and insulin resistance, with great variability in the results of these studies. Studies have suggested that insulin secretion decreases with age while insulin sensitivity remains with age [83] [84]. Our results are in agreement with those of Refaie *et al.* [85] who found that fasting serum insulin was significantly higher in older participants compared to youngers control group, and suggested that insulin resistance would be a hallmark of the normal aging process. This is believed to be the result of a deterioration in both insulin secretion, insulin clearance, and the interaction between insulin and target tissue that occurs with age. Aradillas-García *et al.* found, however, that during childhood and adolescence, insulin concentrations and HOMA-IR exhibited a gradual increase with age [86]. This discrepancy in results may be due to multiple factors, including ethnicity [87] [88] [89] and confounding factors associated with aging such as obesity, decreased physical activity, medications and co-morbidities.

The younger participants more often had a Mdp while the older more often had a Wdp. This result is in disagreement with most of the studies that have addressed the issue of dietary differences between age groups, and who have found rather that the youngest had a westernized diet more often than the older [90] [91]. The study by Hsiao *et al.* Seems to suggest that ethnicity could influence the food preferences of people of the same age group [92], which would explain the discrepancy between our finding and that of the above studies. The following pathophysiological reasoning supports our finding: Aging is associated with a decrease in appetite [93] [94]. This is believed to be due, among other things, to higher circulating concentrations of leptin [93]. The consumption of Westernized diet has been reported to promote the development of central leptin resistance [95] [96]. This is a situation in which the efficacy of the anorexic effect of leptin is decreased, leading to an appetite stimulation [97] [98]. One can imagine that older people prefer the Western diet to compensate for the lack of appetite that occurs with age.

Participants on the Wdp had significantly higher mean insulin and HOMAIR values compared to those on the Mdp. This is in line with other studies [99] [100]. The western diet induced oxydative stress [101], low grade inflammation [102] as well as renin angiotensin stimulation [102] could be the underlying mechanism explaining this correlation.

5. Study Strengths and Limitations

Our study has to be interpreted within the context of its potential strengths and limitations. To the best of our knowledge, this is the first study to investigate the association between salt and specific food consumption as well as different diet patterns with HOMAIR and fasting insulin in sub-Saharan essential hypertensives, taking into account confounding factors such as BMI, WC and especially sedentary time. Nevertheless, although multicentric, the in-hospital design of this study is a limitation, which means that ours results couldn't be extrapolated to the whole hypertensive population. Furthermore, the cross-sectional design could not allow to understand causality of observed relationships and we cannot exclude the possibility of residual confounding.

6. Conclusion

In hypertensive Black sub-Saharan Africans, Salt intake and westernized diet seem to promote insulin resistance whereas Mediterranean diet, fruits, vegetables and fish consumption appear to enhance insulin sensitivity. These results emphasize the importance of nutrition interventions in the management of hypertensive patients. Randomized controlled trials with an adequate study period are needed.

Authors' Contributions

Design and concept of study: KPB, LMB, MKJR;

Acquisition of data: KPB, KZR, LBE, KVE;
Manuscript draft: KPB;
Supervision: KVE, LMB, MKJR;
Statistical analysis: NNA;
All authors read and approved the final manuscript.

Data Availability

Because consent given by study participants did not include data sharing with third parties, anonymized data can be made available to investigators for analysis on reasonable request to the corresponding author.

Conflicts of Interest

The authors had no conflicts of interest to declare in relation to this article.

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References

[1] GBD 2017 Causes of Death Collaborators (2018) Global, Regional, and National Age-Sex-Specific Mortality for 282 Causes of Death in 195 Countries and Territories, 1980-2017: A Systematic Analysis for the Global Burden of Disease Study 2017. *The Lancet*, **392**, 1736-1788.

[2] Monteiro, C.A., *et al.* (2013) Ultra-Processed Products Are Becoming Dominant in the Global Food System. *Obesity Reviews*, **14**, 21-28. https://doi.org/10.1111/obr.12107

[3] Steyn, N.P. and McHiza, Z.J. (2014) Obesity and the Nutrition Transition in Sub-Saharan Africa. *Annals of the New York Academy of Sciences*, **1311**, 88-101. https://doi.org/10.1111/nyas.12433

[4] Misselhorn, A. and Hendriks, S.L. (2017) A Systematic Review of Sub-National Food Insecurity Research in South Africa: Missed Opportunities for Policy Insights. *PLoS ONE*, **12**, e0182399. https://doi.org/10.1371/journal.pone.0182399

[5] Haggblade, S., *et al.* (2016) Emerging Early Actions to Bend the Curve in Sub-Saharan Africa's Nutrition Transition. *Food and Nutrition Bulletin*, **37**, 219-241. https://doi.org/10.1177/0379572116637723

[6] Amegah, A.K. (2018) Tackling the Growing Burden of Cardiovascular Diseases in Sub-Saharan Africa. *Circulation*, **138**, 2449-2451. https://doi.org/10.1161/CIRCULATIONAHA.118.037367

[7] Busnelli, M., *et al.* (2018) Effects of Vegetable Proteins on Hypercholesterolemia and Gut Microbiota Modulation. *Nutrients*, **10**, 1249. https://doi.org/10.3390/nu10091249

[8] Sanchez, A., *et al.* (2019) Diets with Customary Levels of Fat from Plant Origin May Reverse Coronary Artery Disease. *Medical Hypotheses*, **122**, 103-105. https://doi.org/10.1016/j.mehy.2018.10.027

[9] Ozemek, C., *et al.* (2018) The Role of Diet for Prevention and Management of Hypertension. *Current Opinion in Cardiology*, **33**, 388-393. https://doi.org/10.1097/HCO.0000000000000532

[10] Tosti, V., Bertozzi, B. and Fontana, L. (2018) Health Benefits of the Mediterranean Diet: Metabolic and Molecular Mechanisms. *The Journals of Gerontology. Series A, Biological Sciences and Medical Sciences*, **73**, 318-326. https://doi.org/10.1093/gerona/glx227

[11] Gjuladin-Hellon, T., *et al.* (2019) Effects of Carbohydrate-Restricted Diets on Low-Density Lipoprotein Cholesterol Levels in Overweight and Obese Adults: A Systematic Review and Meta-Analysis. *Nutrition Reviews*, **77**, 161-180. https://doi.org/10.1093/nutrit/nuy049

[12] Feinman, R.D., *et al.* (2015) Dietary Carbohydrate Restriction as the First Approach in Diabetes Management: Critical Review and Evidence Base. *Nutrition*, **31**, 1-13. https://doi.org/10.1016/j.nut.2014.06.011

[13] Huffman, M.D. and Lloyd-Jones, D.M. (2017) Global Burden of Raised Blood Pressure: Coming into Focus. *JAMA*, **317**, 142-143. https://doi.org/10.1001/jama.2016.19685

[14] GBD 2017 Mortality Collaborators (2018) Global, Regional, and National Age-Sex-Specific Mortality and Life Expectancy, 1950-2017: A Systematic Analysis for the Global Burden of Disease Study 2017. *The Lancet*, **392**, 1684-1735. https://doi.org/10.1016/S0140-6736(18)31891-9

[15] Bigazzi, R., *et al.* (2008) Increased Cardiovascular Events in Hypertensive Patients with Insulin Resistance: A 13-Year Follow-Up. *Nutrition, Metabolism & Cardiovascular Diseases*, **18**, 314-319. https://doi.org/10.1016/j.numecd.2006.11.001

[16] Ginsberg, H.N. (2000) Insulin Resistance and Cardiovascular Disease. *Journal of Clinical Investigation*, **106**, 453-458. https://doi.org/10.1172/JCI10762

[17] Kraemer, F.B. and Ginsberg, H.N. (2014) Gerald M. Reaven, MD: Demonstration of the Central Role of Insulin Resistance in Type 2 Diabetes and Cardiovascular Disease. *Diabetes Care*, **37**, 1178-1181. https://doi.org/10.2337/dc13-2668

[18] Ormazabal, V., *et al.* (2018) Association between Insulin Resistance and the Development of Cardiovascular Disease. *Cardiovascular Diabetology*, **17**, Article No. 122. https://doi.org/10.1186/s12933-018-0762-4

[19] Manco, M., Calvani, M. and Mingrone, G. (2004) Effects of Dietary Fatty Acids on Insulin Sensitivity and Secretion. *Diabetes, Obesity and Metabolism*, **6**, 402-413. https://doi.org/10.1111/j.1462-8902.2004.00356.x

[20] Hu, F.B. (2011) Globalization of Diabetes: The Role of Diet, Lifestyle, and Genes. *Diabetes Care*, **34**, 1249-1257. https://doi.org/10.2337/dc11-0442

[21] Huneault, L., Mathieu, M.E. and Tremblay, A. (2011) Globalization and Modernization: An Obesogenic Combination. *Obesity Reviews*, **12**, e64-e72. https://doi.org/10.1111/j.1467-789X.2010.00817.x

[22] Olivieri, C. (2019) Combating Insulin Resistance with the Paleo Diet. *The Nurse Practitioner*, **44**, 49-55. https://doi.org/10.1097/01.NPR.0000552683.55684.f8

[23] Kahleova, H., *et al.* (2019) Fat Quantity and Quality, as Part of a Low-Fat, Vegan Diet, Are Associated with Changes in Body Composition, Insulin Resistance, and Insulin Secretion. A 16-Week Randomized Controlled Trial. *Nutrients*, **11**, 615. https://doi.org/10.3390/nu11030615

[24] Golabek, K.D. and Regulska-Ilow, B. (2019) Dietary Support in Insulin Resistance: An Overview of Current Scientific Reports. *Advances in Clinical and Experimental Medicine*, **28**, 1577-1585.

[25] Park, Y.M., *et al.* (2017) Obesity Mediates the Association between Mediterranean Diet Consumption and Insulin Resistance and Inflammation in US Adults. *Journal*

of Nutrition, **147**, 563-571. https://doi.org/10.3945/jn.116.243543

[26] Tsai, S.F., *et al.* (2018) Stress Aggravates High-Fat-Diet-Induced Insulin Resistance via a Mechanism That Involves the Amygdala and Is Associated with Changes in Neuroplasticity. *Neuroendocrinology*, **107**, 147-157. https://doi.org/10.1159/000491018

[27] Small, L., *et al.* (2018) Modeling Insulin Resistance in Rodents by Alterations in Diet: What Have High-Fat and High-Calorie Diets Revealed? *American Journal of Physiology-Endocrinology and Metabolism*, **314**, E251-E265. https://doi.org/10.1152/ajpendo.00337.2017

[28] Antunes, L.C., Elkfury, J.L., *et al.* (2016) Validation of HOMA-IR in a Model of Insulin-Resistance Induced by a High-Fat Diet in Wistar Rats. *Archives of Endocrinology and Metabolism*, **60**, 138-142. https://doi.org/10.1590/2359-3997000000169

[29] Stockli, J., *et al.* (2017) Metabolomic Analysis of Insulin Resistance across Different Mouse Strains and Diets. *The Journal of Biological Chemistry*, **292**, 19135-19145. https://doi.org/10.1074/jbc.M117.818351

[30] Cleland, C.L., *et al.* (2014) Validity of the Global Physical Activity Questionnaire (GPAQ) in Assessing Levels and Change in Moderate-Vigorous Physical Activity and Sedentary Behaviour. *BMC Public Health*, **14**, Article No. 1255. https://doi.org/10.1186/1471-2458-14-1255

[31] Shim, J.S., Oh, K. and Kim, H.C. (2014) Dietary Assessment Methods in Epidemiologic Studies. *Epidemiology and Health*, **36**, e2014009. https://doi.org/10.4178/epih/e2014009

[32] Bonora, E., *et al.* (2000) Homeostasis Model Assessment Closely Mirrors the Glucose Clamp Technique in the Assessment of Insulin Sensitivity: Studies in Subjects with Various Degrees of Glucose Tolerance and Insulin Sensitivity. *Diabetes Care*, **23**, 57-63. https://doi.org/10.2337/diacare.23.1.57

[33] Huang, L., *et al.* (2016) Mean Population Salt Intake Estimated from 24-h Urine Samples and Spot Urine Samples: A Systematic Review and Meta-Analysis. *International Journal of Epidemiology*, **45**, 239-250. https://doi.org/10.1093/ije/dyv313

[34] Ryan, H., Trosclair, A. and Gfroerer, J. (2012) Adult Current Smoking: Differences in Definitions and Prevalence Estimates—NHIS and NSDUH, 2008. *Journal of Environmental and Public Health*, **2012**, Article ID: 918368. https://doi.org/10.1155/2012/918368

[35] Moos, R.H., *et al.* (2009) Older Adults' Alcohol Consumption and Late-Life Drinking Problems: A 20-Year Perspective. *Addiction*, **104**, 1293-1302. https://doi.org/10.1111/j.1360-0443.2009.02604.x

[36] Chiva-Blanch, G., *et al.* (2013) Effects of Red Wine Polyphenols and Alcohol on Glucose Metabolism and the Lipid Profile: A Randomized Clinical Trial. *Clinical Nutrition*, **32**, 200-206. https://doi.org/10.1016/j.clnu.2012.08.022

[37] Ku, P.W., *et al.* (2018) A Cut-Off of Daily Sedentary Time and All-Cause Mortality in Adults: A Meta-Regression Analysis Involving More than 1 Million Participants. *BMC Medicine*, **16**, Article No. 74. https://doi.org/10.1186/s12916-018-1062-2

[38] Campbell, N.R., *et al.* (2015) Proposed Nomenclature for Salt Intake and for Reductions in Dietary Salt. *Journal of Clinical Hypertension* (*Greenwich*), **17**, 247-251. https://doi.org/10.1111/jch.12442

[39] Maugeri, A., *et al.* (2019) How Dietary Patterns Affect Left Ventricular Structure, Function and Remodelling: Evidence from the Kardiovize Brno 2030 Study. *Scientific Reports*, **9**, Article No. 19154. https://doi.org/10.1038/s41598-019-55529-5

[40] The GBD 2015 Obesity Collaborators (2017) Health Effects of Overweight and Ob-

esity in 195 Countries over 25 Years. *The New England Journal of Medicine*, **377**, 13-27. https://doi.org/10.1056/NEJMoa1614362

[41] Whelton, P.K., Carey, R.M., Aronow, W.S., Casey Jr., D.E., Collins, K.J., *et al.* (2018) 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *Hypertension*, **71**, e13-e115. https://doi.org/10.1161/HYP.0000000000000065

[42] O'Connor, S., *et al.* (2019) Impact of a High Intake of Dairy Product on Insulin Sensitivity in Hyperinsulinemic Adults: A Crossover Randomized Controlled Trial. *Current Developments in Nutrition*, **3**, nzz083. https://doi.org/10.1093/cdn/nzz083

[43] Kim, S.H., *et al.* (2015) Association of Insulin Resistance and Coronary Artery Remodeling: An Intravascular Ultrasound Study. *Cardiovascular Diabetology*, **14**, Article No. 74. https://doi.org/10.1186/s12933-015-0238-8

[44] Park, Y.M., *et al.* (2018) An Association of Urinary Sodium-Potassium Ratio with Insulin Resistance among Korean Adults. *Nutrition Research and Practice*, **12**, 443-448. https://doi.org/10.4162/nrp.2018.12.5.443

[45] Ogihara, T., *et al.* (2001) Insulin Resistance with Enhanced Insulin Signaling in High-Salt Diet-Fed Rats. *Diabetes*, **50**, 573-583. https://doi.org/10.2337/diabetes.50.3.573

[46] Fonseca-Alaniz, M.H., Brito, L.C., *et al.* (2007) High Dietary Sodium Intake Increases White Adipose Tissue Mass and Plasma Leptin in Rats. *Obesity* (*Silver Spring*), **15**, 2200-2208. https://doi.org/10.1038/oby.2007.261

[47] Takagi, Y., *et al.* (2018) High-Salt Intake Ameliorates Hyperglycemia and Insulin Resistance in WBN/Kob-$Lepr^{fa/fa}$ Rats: A New Model of Type 2 Diabetes Mellitus. *Journal of Diabetes Research*, **2018**, Article ID: 3671892. https://doi.org/10.1155/2018/3671892

[48] Fonseca-Alaniz, M.H., Takada, J., *et al.* (2008) High Sodium Intake Enhances Insulin-Stimulated Glucose Uptake in Rat Epididymal Adipose Tissue. *Obesity* (*Silver Spring*), **16**, 1186-1192. https://doi.org/10.1038/oby.2008.69

[49] Garg, R., *et al.* (2011) Low-Salt Diet Increases Insulin Resistance in Healthy Subjects. *Metabolism*, **60**, 965-968. https://doi.org/10.1016/j.metabol.2010.09.005

[50] Cui, H., *et al.* (2017) High-Salt Intake Negatively Regulates Fat Deposition in Mouse. *Scientific Reports*, **7**, Article No. 2053. https://doi.org/10.1038/s41598-017-01560-3

[51] Olivares-Reyes, J.A., Arellano-Plancarte, A. and Castillo-Hernandez, J.R. (2009) Angiotensin II and the Development of Insulin Resistance: Implications for Diabetes. *Molecular and Cellular Endocrinology*, **302**, 128-139. https://doi.org/10.1016/j.mce.2008.12.011

[52] Lima, N.K., *et al.* (2009) Salt and Insulin Sensitivity after Short and Prolonged High Salt Intake in Elderly Subjects. *Brazilian Journal of Medical and Biological Research*, **42**, 738-743. https://doi.org/10.1590/S0100-879X2009000800008

[53] Panagiotakos, D.B., *et al.* (2005) The Relationship between Dietary Habits, Blood Glucose and Insulin Levels among People without Cardiovascular Disease and Type 2 Diabetes; The ATTICA Study. *The Review of Diabetic Studies*, **2**, 208-215. https://doi.org/10.1900/RDS.2005.2.208

[54] Pan, A., *et al.* (2011) Red Meat Consumption and Risk of Type 2 Diabetes: 3 Cohorts of US Adults and an Updated Meta-Analysis. *American Journal of Clinical Nutrition*, **94**, 1088-1096. https://doi.org/10.3945/ajcn.111.018978

[55] Ley, S.H., *et al.* (2014) Associations between Red Meat Intake and Biomarkers of Inflammation and Glucose Metabolism in Women. *American Journal of Clinical Nutrition*, **99**, 352-360. https://doi.org/10.3945/ajcn.113.075663

[56] Fretts, A.M., *et al.* (2015) Consumption of Meat Is Associated with Higher Fasting Glucose and Insulin Concentrations Regardless of Glucose and Insulin Genetic Risk Scores: A Meta-Analysis of 50,345 Caucasians. *American Journal of Clinical Nutrition*, **102**, 1266-1278. https://doi.org/10.3945/ajcn.114.101238

[57] Cocate, P.G., *et al.* (2015) Red but Not White Meat Consumption Is Associated with Metabolic Syndrome, Insulin Resistance and Lipid Peroxidation in Brazilian Middle-Aged Men. *European Journal of Preventive Cardiology*, **22**, 223-230. https://doi.org/10.1177/2047487313507684

[58] Pan, A., *et al.* (2013) Changes in Red Meat Consumption and Subsequent Risk of Type 2 Diabetes Mellitus: Three Cohorts of US Men and Women. *JAMA Internal Medicine*, **173**, 1328-1335. https://doi.org/10.1001/jamainternmed.2013.6633

[59] Kim, Y., Keogh, J.B. and Clifton, P.M. (2016) Differential Effects of Red Meat/Refined Grain Diet and Dairy/Chicken/Nuts/Whole Grain Diet on Glucose, Insulin and Triglyceride in a Randomized Crossover Study. *Nutrients*, **8**, 687. https://doi.org/10.3390/nu8110687

[60] Rietman, A., *et al.* (2014) High Dietary Protein Intake, Reducing or Eliciting Insulin Resistance? *European Journal of Clinical Nutrition*, **68**, 973-979. https://doi.org/10.1038/ejcn.2014.123

[61] Floegel, A., *et al.* (2013) Identification of Serum Metabolites Associated with Risk of Type 2 Diabetes Using a Targeted Metabolomic Approach. *Diabetes*, **62**, 639-648. https://doi.org/10.2337/db12-0495

[62] Wang, T.J., *et al.* (2011) Metabolite Profiles and the Risk of Developing Diabetes. *Nature Medicine*, **17**, 448-453. https://doi.org/10.1038/nm.2307

[63] Fernstrom, M., Fernberg, U. and Hurtig-Wennlof, A. (2019) Insulin Resistance (HOMA-IR) and Body Fat (%) Are Associated to Low Intake of Fruit and Vegetables in Swedish, Young Adults: The Cross-Sectional Lifestyle, Biomarkers and Atherosclerosis Study. *BMC Nutrition*, **5**, Article No. 15. https://doi.org/10.1186/s40795-019-0279-6

[64] Miller, V., Yusuf, S., Chow, C.K., Dehghan, M., Corsi, D.J., Lock, K., Popkin, B., Rangarajan, S., Khatib, R., Lear, S.A., Mony, P., Kaur, M., Mohan, V., Vijayakumar, K., Gupta, R., Kruger, A., Tsolekile, L., Mohammadifard, N., Rahman, O., Rosengren, A., Avezum, A., Orlandini, A., Ismail, N., Lopez-Jaramillo, P., Yusufali, A., Karsidag, K., Iqbal, R., Chifamba, J., Oakley, S.M., Ariffin, F., Zatonska, K., Poirier, P., Li, W., Bo, J., Chen, H., Liu, X., Bai, X.L., Te, K. and Mente, A. (2016) Availability, Affordability, and Consumption of Fruits and Vegetables in 18 Countries across Income Levels: Findings from the Prospective Urban Rural Epidemiology (PURE) Study. *The Lancet Global Health*, **4**, E695-E703. https://doi.org/10.1016/S2214-109X(16)30186-3

[65] Du, H., *et al.* (2017) Fresh Fruit Consumption in Relation to Incident Diabetes and Diabetic Vascular Complications: A 7-y Prospective Study of 0.5 Million Chinese Adults. *PLoS Medicine*, **14**, e1002279. https://doi.org/10.1371/journal.pmed.1002279

[66] Abbott, K.A., Burrows, T.L., Acharya, S, Thota, R.N. and Garg, M.L. (2020) DHA-Enriched Fish Oil Reduces Insulin Resistance in Overweight and Obese Adults. *Prostaglandins, Leukotrienes and Essential Fatty Acids*, **159**, Article ID: 102154. https://doi.org/10.1016/j.plefa.2020.102154

[67] Pandey, K.B. and Rizvi, S.I. (2009) Plant Polyphenols as Dietary Antioxidants in Human Health and Disease. *Oxidative Medicine and Cellular Longevity*, **2**, 270-278. https://doi.org/10.4161/oxim.2.5.9498

[68] North, C.J., Venter, C.S. and Jerling, J.C. (2009) The Effects of Dietary Fibre on C-Reactive Protein, an Inflammation Marker Predicting Cardiovascular Disease. *European Journal of Clinical Nutrition*, **63**, 921-933. https://doi.org/10.1038/ejcn.2009.8

[69] Ellulu, M.S., *et al.* (2015) Effect of Vitamin C on Inflammation and Metabolic Markers in Hypertensive and/or Diabetic Obese Adults: A Randomized Controlled Trial. *Drug Design, Development and Therapy*, **9**, 3405-3412. https://doi.org/10.2147/DDDT.S83144

[70] Maleki, S.J., Crespo, J.F. and Cabanillas, B. (2019) Anti-Inflammatory Effects of Flavonoids. *Food Chemistry*, **299**, Article ID: 125124. https://doi.org/10.1016/j.foodchem.2019.125124

[71] Souza, M.T., *et al.* (2014) Structure-Activity Relationship of Terpenes with Anti-Inflammatory Profile—A Systematic Review. *Basic & Clinical Pharmacology & Toxicology*, **115**, 244-256. https://doi.org/10.1111/bcpt.12221

[72] Calder, P.C. (2016) Docosahexaenoic Acid. *Annals of Nutrition and Metabolism*, **69**, 8-21. https://doi.org/10.1159/000448262

[73] Calder, P.C., *et al.* (2017) Health Relevance of the Modification of Low Grade Inflammation in Ageing (Inflammageing) and the Role of Nutrition. *Ageing Research Reviews*, **40**, 95-119. https://doi.org/10.1016/j.arr.2017.09.001

[74] Pi, J., *et al.* (2007) Reactive Oxygen Species as a Signal in Glucose-Stimulated Insulin Secretion. *Diabetes*, **56**, 1783-1791. https://doi.org/10.2337/db06-1601

[75] Saadeh, M., *et al.* (2012) Reactive Oxygen Species Stimulate Insulin Secretion in Rat Pancreatic Islets: Studies Using Mono-Oleoyl-Glycerol. *PLoS ONE*, **7**, e30200. https://doi.org/10.1371/journal.pone.0030200

[76] Yan, Y., *et al.* (2019) Temporal Relationship between Inflammation and Insulin Resistance and Their Joint Effect on Hyperglycemia: The Bogalusa Heart Study. *Cardiovascular Diabetology*, **18**, Article No. 109. https://doi.org/10.1186/s12933-019-0913-2

[77] Park, K., *et al.* (2009) Oxidative Stress and Insulin Resistance: The Coronary Artery Risk Development in Young Adults Study. *Diabetes Care*, **32**, 1302-1307. https://doi.org/10.2337/dc09-0259

[78] Ramalingam, L., *et al.* (2017) The Renin Angiotensin System, Oxidative Stress and Mitochondrial Function in Obesity and Insulin Resistance. *Biochimica et Biophysica Acta (BBA)—Molecular Basis of Disease*, **1863**, 1106-1114. https://doi.org/10.1016/j.bbadis.2016.07.019

[79] Verdile, G., *et al.* (2015) Inflammation and Oxidative Stress: The Molecular Connectivity between Insulin Resistance, Obesity, and Alzheimer's Disease. *Mediators of Inflammation*, **2015**, Article ID: 105828. https://doi.org/10.1155/2015/105828

[80] Houstis, N., Rosen, E.D. and Lander, E.S. (2006) Reactive Oxygen Species Have a Causal Role in Multiple Forms of Insulin Resistance. *Nature*, **440**, 944-948. https://doi.org/10.1038/nature04634

[81] Ma, Q., *et al.* (2016) Association between Glycated Hemoglobin A1c Levels with Age and Gender in Chinese Adults with No Prior Diagnosis of Diabetes Mellitus. *Biomedical Reports*, **4**, 737-740. https://doi.org/10.3892/br.2016.643

[82] Murphy, W.G. (2014) The Sex Difference in Haemoglobin Levels in Adults—Me-

chanisms, Causes, and Consequences. *Blood Reviews*, **28**, 41-47. https://doi.org/10.1016/j.blre.2013.12.003

[83] Zhu, H.Q., *et al.* (2012) [Ageing Related Changes of Insulin Secretion and Insulin Sensitivity among Normal Glucose Tolerance Individuals in China]. *National Medical Journal of China*, **92**, 1948-1953.

[84] Akehi, Y., *et al.* (2007) [The Effects of Age on Insulin Sensitivity and Insulin Secretion in Japanese Subjects with Normal Glucose Tolerance]. *Rinsho Byori*, **55**, 901-905.

[85] Refaie, M.R., Sayed-Ahmed, N.A., Bakr, A.M., Abdel Aziz, M.Y., El Kannishi, M.H. and Abdel-Gawad, S.S. (2006) Aging Is an Inevitable Risk Factor for Insulin Resistance. *Journal of Taibah University Medical Sciences*, **1**, 30-41. https://doi.org/10.1016/S1658-3612(06)70005-1

[86] Aradillas-Garcia, C., *et al.* (2012) Distribution of the Homeostasis Model Assessment of Insulin Resistance in Mexican Children and Adolescents. *European Journal of Endocrinology*, **166**, 301-306. https://doi.org/10.1530/EJE-11-0844

[87] Ladwa, M., *et al.* (2019) A Systematic Review of Beta Cell Function in Adults of Black African Ethnicity. *Journal of Diabetes Research*, **2019**, Article ID: 7891359. https://doi.org/10.1155/2019/7891359

[88] Tan, V.M., *et al.* (2015) Ethnic Differences in Insulin Sensitivity and Beta-Cell Function among Asian Men. *Nutrition & Diabetes*, **5**, e173. https://doi.org/10.1038/nutd.2015.24

[89] Inaishi, J. and Saisho, Y. (2017) Ethnic Similarities and Differences in the Relationship between Beta Cell Mass and Diabetes. *Journal of Clinical Medicine*, **6**, 113. https://doi.org/10.3390/jcm6120113

[90] Olmedo-Requena, R., *et al.* (2014) Factors Associated with a Low Adherence to a Mediterranean Diet Pattern in Healthy Spanish Women before Pregnancy. *Public Health Nutrition*, **17**, 648-656. https://doi.org/10.1017/S1368980013000657

[91] Inelmen, E.M., *et al.* (2008) Differences in Dietary Patterns between Older and Younger Obese and Overweight Outpatients. *The Journal of Nutrition*, *Health & Aging*, **12**, 3-8. https://doi.org/10.1007/BF02982157

[92] Hsiao, P.Y., *et al.* (2013) Dietary Patterns and Diet Quality among Diverse Older Adults: the University of Alabama at Birmingham Study of Aging. *The Journal of Nutrition*, *Health & Aging*, **17**, 19-25. https://doi.org/10.1007/s12603-012-0082-4

[93] Johnson, K.O., *et al.* (2020) Differences in Circulating Appetite-Related Hormone Concentrations between Younger and older Adults: A Systematic Review and Meta-Analysis. *Aging Clinical and Experimental Research*, **32**, 1233-1244. https://doi.org/10.1007/s40520-019-01292-6

[94] Pilgrim, A.L., *et al.* (2015) An Overview of Appetite Decline in Older People. *Nursing Older People*, **27**, 29-35. https://doi.org/10.7748/nop.27.5.29.e697

[95] Sample, C.H., *et al.* (2015) Western-Style Diet Impairs Stimulus Control by Food Deprivation State Cues: Implications for Obesogenic Environments. *Appetite*, **93**, 13-23. https://doi.org/10.1016/j.appet.2015.05.018

[96] de Git, K.C. and Adan, R.A. (2015) Leptin Resistance in Diet-Induced Obesity: The Role of Hypothalamic Inflammation. *Obesity Reviews*, **16**, 207-224. https://doi.org/10.1111/obr.12243

[97] Friedman, J. (2016) The Long Road to Leptin. *Journal of Clinical Investigation*, **126**, 4727-4734. https://doi.org/10.1172/JCI91578

[98] Farooqi, I.S. and O'Rahilly, S. (2014) 20 Years of Leptin: Human Disorders of Lep-

tin Action. *Journal of Endocrinology*, **223**, T63-T70.
https://doi.org/10.1530/JOE-14-0480

[99] Fung, T.T., *et al.* (2001) Association between Dietary Patterns and Plasma Biomarkers of Obesity and Cardiovascular Disease Risk. *American Journal of Clinical Nutrition*, **73**, 61-67. https://doi.org/10.1093/ajcn/73.1.61

[100] Shively, C.A., *et al.* (2019) Mediterranean versus Western Diet Effects on Caloric Intake, Obesity, Metabolism, and Hepatosteatosis in Nonhuman Primates. *Obesity* (*Silver Spring*), **27**, 777-784. https://doi.org/10.1002/oby.22436

[101] Erdelyi, I., *et al.* (2009) Western-Style Diets Induce Oxidative Stress and Dysregulate Immune Responses in the Colon in a Mouse Model of Sporadic Colon Cancer. *Journal of Nutrition*, **139**, 2072-2078. https://doi.org/10.3945/jn.108.104125

[102] Kopp, W. (2019) How Western Diet and Lifestyle Drive the Pandemic of Obesity and Civilization Diseases. *Diabetes*, *Metabolic Syndrome and Obesity*, **12**, 2221-2236. https://doi.org/10.2147/DMSO.S216791