General Medicine Open

Research Article

ISSN: 2515-4737

Mediterranean diet and metabolic syndrome in three countries of Calabria

Cornelli U[1]*, Cassano G[2], Meringolo G[3], Rausa M[4], Valente O[5] and Recchia M[6]

[1]Loyola University School of Medicine, Chicago, USA

[2]MAP (Monitoring Alimentary Pathology center, Rende, Italy

[3]Department of Cardiology, Rende Hospital, Italy

[4]Department of Public Health, Rende, Italy

[5]Municipal administration, Rovito, Italy

[6]Statistical Dept University of Lugano, Switzerland

Abstract

Mediterranean diet has been associated with low prevalence and progression of metabolic syndrome (MetS). However, no specific foods have been described as causative of MetS.

Six hundred subjects of both sexes (between 35-65 years) have been studied in the investigational centers of MAP (Monitoraggio Alimenti Patologia) organized by the local Municipalities of three countries in Calabria-Italy. The enrollment was suggested by family doctors who were addressing subjects suffering from MetS matched with subject non MetS in the same age range. Food intake was analyzed through a weakly questionnaire (FIA or Food Intake assessment).

529 subjects (85 MetS/297 females, and 75 MetS/232 males) concluded the study. In both genders cardiovascular diseases and ultrasound carotid damages were significantly higher, and in males osteoarthosis also was more frequent. Caloric intake was significantly more consistent in MetS with no distinction among carbohydrates, proteins, fibers or fats but with different food pattern in females and males.

Among 77 different foods, in females more white meat, less carrots, cauliflower and red wine were found in MetS. In males red wine, beer, garlic, milk, salami, fruit of the season, and chocolate were lower in MetS and canned tuna was higher.

Multivariate analysis indicate that a complex food combination is determining MetS, with different figures for males and females.

In an area typical for the Mediterranean diet, MetS seems determined by an excessive caloric intake with different food pattern depending upon the gender, indicating that it is not possible to generalize about diet components as causative of the disease.

Introduction

Metabolic syndrome (MetS) is a multi-factorial disorder including hyperglycemia, dyslipidemia, hypertension, and abdominal obesity that is becoming one of the most common pathologies affecting the adult worldwide in a similar proportion for both genders [1,2].

Despite some argument about its role and value in clinical practice, subjects presenting the three of the 5 components as defined by the ATP III (Adult Panel Treatment III) consisting of the increase of blood glucose, triglycerides, blood pressure, abdominal circumference, and reduction of HDL cholesterol, have five times risk or more for type 2 diabetes mellitus, three times risk of developing coronary heart attack or stroke, and two times higher cardiovascular mortality than subjects without the syndrome [1,3].

Considering the pathophysiology, overweight and obesity are central to the risk of the disease predisposing to the insulin resistance, hypertension and dyslipidemia.

Evidence of genetic component have been suggested in term of heritability: family studies provided information about a consistent heritability of some component; linkage studies have shown combinations among the different determinants (e.g, HDL, blood pressure, triglyceride, abdominal visceral fats) in Caucasian, African-American, Mexican-American; genoma wide association studies (GWAS) have detected some single nucleotide polymorphism of fat mass and obesity associated protein (FTO) [4-8].

The inflammatory condition and modification of the gut microbiota are also considered as causative and witness the complexity of the disease [9,10].

The prevalence of MetS is increasing despite a large difference between countries estimated from 10 to 84 % depending on the ethnicity, age, gender, and race of the population [11]. Accompanied to a rapid increase of the life expectancy, it is estimated that around a quarter of the world's adult population has MetS.

***Correspondence to:** Umberto Cornelli, Loyola University School of Medicine, Chicago, 2160 First Ave Maywood IL, Piazza Novelli 5 20129 Milan, Italy, E-mail: ucornelli@gmail.com

***Key words:** mediterranean diet, metabolic syndrome, calabria*

Received: November 20, 2018; **Accepted:** December 03, 2018; **Published:** December 06, 2018

The major risk factor for developing the disease are considered to be the diet rich in fats and carbohydrates and physical inactivity [1,2].

However, among carbohydrates and lipids many distinctions have been made.

For carbohydrates, although they are the only foods constituents that directly increase blood glucose, a distinction has to be made between those with high glycemic index (GI) or glycemic load (GL) -as refined grains, potatoes and sugar sweetened beverages- from other foods as the minimally processed grains, legumes, whole fruits and also pasta in that they do not have a sudden impact on insulin release because of the hifgh fiber content [12]. At the end the quality of carbohydrates seems to have a more important role than the quantity.

The same is for lipids, because saturated fats have different metabolic activity compared to unsaturated lipids which behave differently depending upon the degree of unsaturation as for seed oil, extravirgin olive oil, palm oil. Even more the production process to refine oils can generate toxic compounds as for palm oil.

Lifestyle modification is considered one of the keys to counteract the MetS.

In a meta-analysis of some randomized controlled study on lifestyle modification was shown that the adherence to a healthy diet or a combination of diet and physical activity increase were associated with the reversion of MetS [13]. Talking about healthy diet, in a meta-analysis of several studies (50) -consisting in total of > 500.000 subjects- the Mediterranean diet was shown to be appropriate by all the population groups for primary and secondary prevention of the disease [14,15].

Italy, Spain, Serbia, Greece -just to mention some of the countries on the Mediterranean Sea- use to eat very different foods, or similar foods with different recipe. Despite the common use of extra virgin olive oil, fruit and vegetables in this diet one may consider also that countries are not comparable in terms of MetS prevention or treatment due to environment and lifestyle differences.

The consequence of all these distinctions is that the total amount of food components in the diet such as carbohydrates, lipids, proteins, fibers do not give enough information on the MetS development.

Even more, the same components in different area of the same country may have a different impact. In other terms, is almost impossible to draw conclusion about the effect of foods in determining the MetS unless a restricted territory will be analyzed where subjects are used to eat similar food and similar traditional way of preparing foods.

For this reason, after having crossed the Italy with a mobile unit [16] we decided to choose an Italian region (Calabria) where to start an observational study in different towns controlling the food intake in subjects with MetS compared to matched non MetS people. The aim was to identify what kind of food if any was relating to the disease using a weekly validated Food Intake questionnaire (FIA) consisting of 250 different foods [17].

Material and methods

This research represents a pilot study of the three countries aimed to drive the long-term study (10 years) that will consider the relationship between Foods and MetS (called MAP or Monitoraggio Alimenti Patologia) in ten countries of Calabria-Italy. The data concerning the first evaluation of 600 cases were evaluated.

Three countries were selected: Rovito which is located on a hill, San Lucido on the sea side, and Rende on the plain.

Enrollment method

A conference on "food and pathology" open to the public was organized in three towns (Rovito, San Lucido, and Rende) with the aid of the relative Municipalities. Family doctors were asked to participate and requested to help in the enrollment of their patients suffering from MetS matched with other non-MetS subjects coming for a routine check out.

The enrolment duration was three month/town in the same period of the year and in total the study lasted 3 years. The Ethical Committees of the three Municipalities involved approved the protocol.

Admission criteria

Subject of both sexes aging between 35 and 60 years were admitted suffering from MetS matched with subjects suffering from other diseases provided that only one of the 5 typical variables of MetS (according to ATP III or Adult Treatment Panel) was present. The capacity to fill up correctly the FIA (weakly Food Intake Assessment-see later) after the training was a prerequisite to enter the study.

Exclusion criteria

Cancer of any type, severe psychiatric or metabolic disorders, chronic diseases not under adequate therapy control, more than one variable of MetS according to ATP III, FIA questionnaire unreliable.

FIA questionnaire

FIA consisted of a list of the most common 250 foods in Italy [17]. Following a training with a nutritionist the subject had to fill up a 7 days questionnaire recording the amount (in g or mL) of each of the listed foods. The questionnaire was fundamental for the study, and subjects presenting records with a caloric intake lower than 90 % of the Mifflin St Jeor (MSJ) were excluded. However, the latter were excluded from the current evaluation but continued study.

The FIA was taken at least twice in the period of two years of observation and the data were reported as averages.

Smokers were included in the study and were considered as current smokers or nonsmokers. The latter where those subjects with at least 5 years of interruption. Physical activity was measured through a very simple 4 points questionnaire considering the following items: sedentariness, limited activity, normal activity, physical training.

Lab analysis and anthropometric measures, echography

The common variables for MetS according to ATP III were measured consisting of HDL, triglycerides (TG), blood pressure (BP), abdominal circumference (AC), and glucose. Blood samples were taken before the enrollment to confirm the diagnosis.

The enrolled subjects underwent to the ultrasound carotid analysis using VIVID L8 ultrasound machine. The degree of the arterial lesion was according to a classification into VI different classes: from Class I (normal artery) to class VI (presence of complex plaques with stenosis) [18].

Statistical analysis

Sample

The number of cases to be enrolled was on heuristic base to analyzes the possibility continue the long-term study and in case to adapt the protocol. Two hundred cases for each country (600 cases in total) were analyzed considering obtaining valuable data in at least 500 cases. With these figures, the hypothesis was to analyze about 30

% of the cases with a MetS. However, to be sure to obtain at least 150 cases of MetS, the family doctors were asked to make a first selection consisting of one case of MetS (no matter about the sex) and two matched patients non MetS provided within the admission criteria.

Calculations

Each variable was analyzed calculating the average and SD. The t test or Wilcoxon test were used to determine the relative differences between groups (MetS, Vs non MetS defined as "Controls") for all the variables. The frequencies of concomitant diseases in the two groups were measured using the chi square test (Fisher, with or without Yates correction).

For what concern the FIA, the average weekly data (of two FIA taken within the period) for any food (e.g. pasta, wine, red meat) were determined only to have a rough indication of the quantities (in g or mL). Following the control of the variables distribution, the category analysis was based on discretization (D) of each variable using from 2 to 5 (or D2-D5) different cut off. The Pearson chi square was used to differentiate the two groups followed by the Nominal Logistic Fit value.

For each food, odds ratios were analyzed to compare the differences between various D levels comparing controls and MetS. The logistic regression model (Likelihood Ratio test) was applied to analyze the connection between foods within MetS and controls to describe which were more frequent in MetS compared to controls [19].

Results

In the three selected countries Rovito, San Lucido and Rende a total of 600 subjects were analyzed.

The flow chart of the study is reported in Table 1.

The percentages of MetS in the three towns were respectively 32.6 % in Rovito, 31.6 % in San Lucido, and 26.7 % in Rende. These values indicate that the family doctors were making a similar selection of the cases.

The compliance of the study was 88 % since only 529 subjects concluded correctly the questionnaire. Seventy-one were excluded: 47 because of an incorrect FIA, and 24 were not returning at all the FIA.

The general characteristics of the subjects are reported in Table 2. The caloric intake measured through FIA analysis was between the 96% to 98 % of the theoretical intake calculated according to the MSJ formula.

The differences between controls and MetS subjects were statistically significant (t test $p < 0.05$) for all the variables that are typical of the syndrome.

Total and LDL cholesterol in male with MetS was found lower than in controls despite the differences were not statistically significant (t test $p > 0.05$). This could be due to the treatment of dyslipidemia that was more common in these subjects than in control group (respectively 9.3% Vs 5.1 %: see Table 3).

The total caloric intake measured according to FIA was significantly higher in both groups with MetS and similar to the respective MSJ formula (the differences were < 4 %).

For what concerns the concomitant diseases, in the group of MetS the number of subjects suffering from cardiovascular disease was significantly higher (chi square $p < 0.01$) in both males and females (Table 3). This was confirmed by the ultrasound analysis (ECO) where class IV images (presence of small plaques) were higher in both groups of MetS although the difference was significant in males only (chi square test $p < 0.05$). The percentages of all the other diseases were similar, a part of osteroarthrosis that was present with significantly higher incidence in males only.

In males a higher incidence of total diseases/person in the groups of MetS was found, the differences were statistically significant (Wilcoxon test $p < 0.05$). In females the total disease/person were slowly higher (+ 12.4 %) but not statistically significant (Wilcoxon test $p > 0.05$).

Considering the main food components, the only difference between groups was detected for proteins intake with a significant increase in males with MetS, and surprisingly a lower intake of alcohol (mainly due to lower red wine drinking) was shown (Table 4). Carbohydrates and lipids do not present any important difference between groups as for the fibers. The ratio carbohydrates/lipids or soluble sugars/lipids in term of caloric intake were not significantly different in both sexes.

Table 1. Enrollment flow chart

	Towns			Total
	Rovito	San Lucido	Rende	
Subjects	200	200	200	600
Drop out (no FIA report)	3	15	6	24
FIA Incorrect	13	27	7	47
Total non-included	16	42	13	71
Females Controls	72	69	71	212
Females with MetS	30	38	17	85
Male controls	52	39	66	157
Male with MetS	30	12	33	75
Total females	102	107	88	297
Total males	82	51	99	232
Total evaluated	184	158	187	529

Table 2. General characteristics of the subjects: mean values ± SD or frequencies

Gender		Females				Males			
Disease [N of cases]		Controls [212]		MetS [85]		Controls [157]		MetS [75]	
Variables	Measure	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Age	Years	47.5	6.95	47.5	7.97	50.0	7.98	51.9	8.35
Height	m	1.58	0.055	1.59	0.054	1.70	0.061	1.71	0.072
Weight	Kg	66.1	11.26	79.9[a]	15.7	80.2	11.59	89.9[a]	11.70
BMI	Kg/m^2	26.6	4.69	31.7[a]	5.37	27.9	3.26	30.7[a]	3.87
AC	cm	87.9	13.93	102.4[a]	19.42	97.1	13.68	105.4[a]	25.45
BP min	mmHg	82	27.0	87[a]	28.3	82	28.3	88[a]	35.9
BP mx	mmHg	129	47.8	139[a]	46.7	132	50.4	140[a]	49.8
Total CH	mg/dL	205	37.9	212	41.6	214	37.7	204	36.6
LDL	mg/dL	126	33.2	138[a]	40.4	137	34.6	130	36.4
HDL	mg/dL	61	11.5	46[a]	11.1	51	9.9	40[a]	11.2
Triglycerides	mg/dL	101	34.5	175[a]	63.5	134	57.8	245[a]	153.3
Glucose	mg/dL	88	10.8	94[a]	16.8	93	13.6	103[a]	29.0
Smoking	Yes/no	12/200		5/85		8/149		5/70	
Physical activity [b]	S/O	195/17		77/8		150/7		8/69	
MSJ [c]	Kcal/week	11751	1479.1	12923	1511.8	15437	1659.2	16136	1882.0
Calorie intake [d]	Kcal/week	11304	4021.4	12378	4892.0	15045	5043.1	15752	4855.4

[a] t test Controls Vs MetS $p < 0.05$; [b] S = sedentariness and O = limited activity, normal activity, physical training; [c] Caloric intake using Mifflin St Jeor formula; [d] Caloric intake calculated from the FIA

Table 3. Concomitant diseases: percentage of the total subjects

Gender	Females		Males	
Disease [N of cases]	Controls [212]	MetS [85]	Controls [157]	MetS [75]
Concomitant disease	%	%	%	%
Allergic	1.9	1.2	2.5	4.0
Bronchopulmonary	0.5	0	0	0
Cardiovascular	13.2	29.4[a]	15.3	38.7[a]
Dyslipidemic	4.7	3.5	5.1	9.3
Dermatological	0.5	0	0.5	0
Endocrinological	10.4	10.5	1.3	2.7
ENT	0.5	1.2	0	0
Gastroenterological	3.3	7.1	2.5	8.0
Gynecological	0.9	0	-	-
Hematological	0.9	2.4	0	2.7
Osteoarthritic	58.0	50.6	31.8	45.3[a]
Odonatological	1.4	1.2	0	2.7
Ophthalmological	1.4	1.2	0	0
Neurological	3.3	4.7	0.6	1.3
Psychiatric	0.9	3.5	0	1.5
Urological	-	-	3.2	6.7
Cancer [b]	2.8	0	0	0
EC0 class IV	5.7	11.8	3.8	14.7 [a]
Total/person	1.10	1.24	0.6	1.30
% increase Vs control		13		117

[a] Chi square $p < 0.05$; [b] no malignancy

The analysis of food intake was conducted for all the 250 foods reported in the FIA (Food Intake Assessment). Seventy-seven type of food were measured (see Table 5) and the others up to 250 were not used or reported.

Following a careful analysis of foods distribution, for each item an arbitrary classification (discretization) was settled in terms of cut off forming from 2 to 5 different classes (Table 5).

Some of the listed foods in FIA were not part of the usual diet of the area or were used by few subjects only (e.g. mushrooms, pumpkin, pate, wurstel, big burghers, canned soup) and were not considered in the analysis. In total, the caloric intake of the foods listed accounted for at least the 90% of the total caloric amount/subject (Table 5).

The percentages of subjects within the given discretization were summarized together with the relative statistical analysis to compare controls and MetS subjects (Table 6).

The following results were found:

-for the carbohydrates-based foods, in females no differences were shown between controls and MetS, whereas in males the biscuits intake

Table 4. Main food components as percentage of the total caloric intake and ratios with lipids: Mean ± SD

Gender	**Females**				**Males**			
Disease	Controls		MetS		Controls		MetS	
Components	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Carbohydrates	23.3	13.57	20.3	15.76	23.2	16.02	24.6	15.14
Soluble sugars	26.3	12.72	29.3	17.16	25.1	15.28	24.7	13.53
Proteins	16.3	2.86	16.8	4.25	16.0	2.96	16.7[a]	2.26
Lipids	33.8	5.98	33.6	6.90	31.0	6.13	31.4	6.28
Alcohol	1.5	2.05	1.1	1.90	5.4	4.30	3.7[a]	4.53
Fiber g/week	93	43.8	95	61.1	102	42.8	98	52.6
Ratio carbohydrates/lipids	0.72	0.469	0.62	0.517	0.78	0.585	0.88	0.758
Ratio soluble sugars/lipids	0.82	0.526	0.91	0.560	0.86	0.630	0.82	0.484

[a]= t test Controls Vs MetS $p < 0.05$

Table 5. Average intake (g or mL) of different foods in Females (F) and Males (M) in the two groups of subjects, Controls and MetS, and relative discretization cut off for the different foods

Food	**Controls means**	**MetS means**	**Discretization categories and cut off values [a]**					
	F/M	F/M	0	1	2	3	4	5
Carbohydrates based food								
Biscuits	68/52	54/40	0	40	140	280	480	-
Bread	433/587	456/550	0	200	450	950	2550	-
Breadsticks	4/4	8/2	0	20	100	280	-	-
Croissant	80/73	80/68	0	75	275	700	-	-
Crackers	17/10	22/7	0	40	80	280	-	-
Gnocchi	13/23	15/14	0	3	50	80	-	-
Oatmeal	10/8	15/8	0	80	280	600	-	-
Rusks	45/26	62/26	0	40	80	140	420	-
Sandwich homemade	85/107	55/97	0	40	280	1120	-	-
Sandwich commercial	13/22	21/21	0	54	315	630	-	-
Pasta	304/404	302/402	0	182	395	690	1200	-
Polenta	5/1	7/3	0	30	122	360	-	-
Pizza	153/163	153/140	0	34	150	422	1470	-
Potatoes	75/63	42/63	0	75	300	1060	-	-
Rice	50/50	55/49	0	25	145	280	560	-
Tortellini	11/13	15/9	0	25	100	240	-	-
Fruits								
Apples	476/560	457/539	0	200	700	1400	4200	-
Banana	217/230	189/171	0	199	600	2800	-	-
Citrus fruit	500/542	360/498	0	200	1700	4000	-	-
Dried fruit	97/81	73/114	0	80	280	1900	-	-
Fruit in syrup	8/20	22/1	0	18	100	1050	-	-
Fruit of the season [b]	460/521	673/491	0	475	950	1450	4000	-
Fruit Juice mL	48/35	65/104	0	75	450	2100	-	-
Grapes	65/43	72/41	0	50	300	2350	-	-
Homemade juice mL	90/74	85/130	0	75	160	300	-	-
Pineapple	30/18	43/35	0	68	300	495	-	-
Plums	1/2	1/0	0	20	150	180	-	-
Vegetables/pulses								
Carrots	47/41	36/33	0	40	140	690	-	-
Cauliflower	56/33	40/35	0	60	260	1820	-	-
Celery	19/11	21/12	0	3	140	330	-	-
Chicory/lettuce	187/193	160/194	0	90	245	490	500	1170
Fennels	108/93	70/124	0	480	2000	3380	-	-
Garlic	1.6/1.7	1.7/1	0	1.5	7	20	-	-
Onions	82/83	70/61	0	90	290	630	-	-
Pepper	61/68	100/52	0	50	250	1750	-	-
Pulses dry	21/27	21/25	0	45	90	225	-	-
Pulses canned	36/37	33/33	0	19	160	240	400	-
Savoy cabbage	40/43	50/45	0	15	320	1280	-	-
Soy germ	2/0	0/0	0	30	210	-	-	-
Spinach	93/76	87/54	0	80	350	1440	-	-

Tomato	326/367	320/360	0	60	340	820	2450	-
Zucchini	149/93	175/153	0	100	280	500	1890	-
Beverages								
Spirits	5.5/32	3.6/17	0	80	300	560	-	-
Beer mL	108/319	128/205	0	240	760	3750	-	-
Coffee mL	250/267	247/282	0	195	280	480	1280	-
Sweet beverages mL	272/382	402/356	0	1980	3000	11880	-	-
Tea	1.9/4.4	2.6/1.1	0	1	5	21	210	-
Water [L]	6.3/6.8	7.1/7.3	0	2.8	5.8	8.5	21.0	-
Wine white mL	25/93	27/36	0	65	380	1820	-	-
Wine red mL	157/609	92/415	0	65	325	800	4400	
Meat, processed meat, and fish								
White meat	171/178	293/201	0	50	190	380	980	-
Red meat	201/260	209/216	0	100	140	400	-	-
Salami	124/184	117/135	0	75	170	280	340	820
Offal	13/14	6/13	0	50	140	340	-	-
Bacon	16/28	24/12	0	26	80	160	-	-
Ham	70/63	53/76	0	30	120	250	700	-
Speck	3/8	6/8	0	30	90	180	-	-
Fish	206/224	202/230	0	70	140	700	1400	-
Canned tuna	24/23	19/53	0	24	82	180	800	-
Dairy products								
Milk mL	846/639	707/412	0	400	900	1400	2800	4800
Cheese	149/181	145/168	0	95	190	295	635	-
Ice cream	38/41	50/54	0	25	75	125	700	-
Mozzarella	70/67	76/72	0	25	75	160	640	-
Ricotta cheese	37/30	35/34	0	25	70	120	490	-
Yogurt	107/61	90/78	0	60	360	1680	-	-
Eggs	57/61	55/60	0	25	125	350	700	-
Dressing								
Butter	7/7	6/8	0	40	160	270	-	-
Mayonnaise	2/4	4/1	0	5	21	320	-	-
Margarine	1/1	2/2	0	10	140	-	-	-
Olive oil	108/105	104/104	0	100	180	405		
Desserts								
Homemade jam	10/11	13/12	0	20	40	210	-	-
Honey	1/1	3/1	0	3	35	85	-	-
Chocolate	17/19	17/9	0	15	55	210	-	-
Cake	149/155	149/107	0	35	175	560	1330	-
Other foods miscellanea								
Sweeteners	1.1/1.0	0.9/2.2	0	1	5	7	21	-
Salt added	25/25	24/23	0	12	22	35	43	140
Sugar added	37/31	35/33	0	14	31	75	270	-

[a] example: biscuits - discretization category 1 (from 0 to 40 g); category 2 (from 40 g to 140 g); category 3 (from 140 g to 280 g); category 4 (from 280 g to 480 g); [b] Fruit of the season: mainly figs, peaches, apricot, strawberry, pear, and cherries.

was significantly lower in MetS group with a Nominal Logistic Fit value (NLF) of p = 0.03804.

-for fruits, in the female groups no significant differences were found between groups, whereas in males with MetS the intake of the fruit of the season was found significantly lower (NLF p = 0.04556)

-for vegetables, in the females group with MetS differences were found in the carrots and cauliflowers intakes which were significantly lower with MetS (respectively an NLF with p = 0.03182 and 0.03796). In the males group garlic and carrots intakes were significantly lower, respectively with an NFT with p = 0.01764 and 0.04715.

-for beverages, in the females group with MetS the red wine intake was significantly lower (NLF p = 0.00232) and in man the red wine and beer intakes were significantly lower in the MetS group (respectively NLF p = 0.03694 and 0.04853).

-For meat, processed meat and fish categories, in females with MetS the white meat intake was significantly higher than Controls (NFT p = 0.01515), whereas for all the other foods within the categories no significant differences were detected. For males the intakes of salami and offal were significantly lower in MetS group (respectively NFT p = 0.02932 and 0.0414), whereas in the same group the canned tuna consumption was much higher (NFT p = 0.03473).

- For dairy derivatives, in females no differences were found between the two groups, whereas in males the milk intake was significantly lower in the MetS subjects (NFT p = 0.04176).

-In the miscellanea group, no differences between MetS and Controls were found a part of chocolate whose intake was lower in males of the MetS group (NFT p = 0.0397).

All the differences determined through the NFT were confirmed by the relative analysis of the Odds Ratios.

Table 6. Percentages of subject in each discretization category (from D1 to D5) divided by sex

Gender	**Female**										**Male**									
Disease	**Controls**					**MetS**					**Controls**					**MetS**				
Discretization [D]	1	2	3	4	5	1	2	3	4	5	1	2	3	4	5	1	2	3	4	5
Carbohydrates based foods																				
Biscuits	42	38	17	3	-	55	29	13	3	-	58	29	9	4	-	67	19	13	1	- **a**
Bread	25	33	34	8	-	17	38	36	9	-	15	24	45	16	-	9	32	49	9	-
Breadsticks	92	6	2	-	-	94	4	2	-	-	92	6	1	-	-	92	8	0	-	-
Croissant	76	21	3	-	-	80	15	5	-	-	80	15	5	-	-	77	21	1	-	-
Crackers	83	7	10	-	-	80	9	11	-	-	90	5	5	-	-	92	5	3	-	-
Gnocchi	83	0	7	10	-	81	1	8	10	-	78	1	6	14	-	83	1	3	13	-
Oatmeal	91	8	1	-	-	94	4	2	-	-	97	2	1	-	-	95	5	0	-	-
Rusks	66	8	10	15	-	55	9	13	23	-	78	6	7	9	-	79	7	5	9	-
Sandwich homemade	63	24	12	1	-	65	28	6	1	-	61	26	11	2	-	60	24	13	3	-
Sandwich commercial	90	8	1	-	-	88	10	2	-	-	89	9	2	-	-	88	10	2	-	-
Pasta	26	49	21	4	-	30	38	30	2	-	15	41	37	7	-	12	41	36	11	-
Polenta	96	3	1	-	-	96	2	1	-	-	99	1	0	-	-	97	1	1	-	-
Pizza	31	30	36	3	-	26	41	31	2	-	28	34	34	4	-	33	32	33	1	-
Potatoes	75	19	6	-	-	83	11	6	-	-	81	10	9	-	-	77	17	5	-	-
Rice	48	43	8	1	-	50	41	7	2	-	51	39	6	4	-	55	35	11	0	-
Tortellini	87	9	3	-	-	81	14	5	-	-	85	11	4	-	-	89	7	4	-	-
Fruits																				
Apples	42	28	21	9	-	39	33	17	11	-	39	27	17	17	-	43	21	20	16	-
Banana	55	30	15	-	-	57	32	11	-	-	59	23	8	-	-	63	27	10	-	-
Citrus fruit	44	49	7	-	-	56	38	6	-	-	41	51	8	-	-	49	45	5	-	-
Dried fruit	69	21	10	-	-	57	25	8	-	-	70	18	12	-	-	66	23	11	-	-
Fruit in syrup	95	0	5	-	-	89	0	11	-	-	94	0	6	-	-	99	0	1	-	-
Fruit of the season [b]	62	18	12	8	-	57	13	15	14	-	60	16	15	9	-	71	7	9	13	- **a**
Fruit juice	95	5	-	-	-	94	6	-	-	-	95	4	1	-	-	88	9	3	-	-
Grapes	81	10	9	-	-	82	10	8	-	-	83	8	9	-	-	91	2	7	-	-
Homemade fruit juice	88	7	5	-	-	86	8	6	-	-	89	7	4	-	-	83	9	8	-	-
Pineapple	87	11	2	-	-	83	13	4	-	-	92	7	1	-	-	84	11	5	-	-
Plums	98	2	0	-	-	96	4	0	-	-	99	0	1	-	-	99	1	0	-	-
Vegetables and pulses																				
Carrots	58	32	10	-	-	71	20	8	-	- **a**	63	27	10	-	-	70	27	3	-	- **a**
Cauliflower	73	16	11	-	-	87	9	4	-	- **a**	82	12	6	-	-	81	15	4	-	-
Celery	74	22	4	-	-	78	17	5	-	-	85	12	3	-	-	88	7	5	-	-
Chicory/lettuce	31	42	21	1	5	36	33	25	2	4	27	41	25	3	4	35	37	20	1	7
Fennels	92	8	-	-	-	96	4	-	-	-	92	8	0	-	-	95	4	1	-	-
Garlic	63	30	7	-	-	60	33	7	-	-	62	31	7	-	-	77	19	4	-	- **a**
Onions	62	32	6	-	-	65	30	5	-	-	60	34	6	-	--	64	31	5	-	-
Pepper	72	20	8	-	-	68	20	13	-	-	72	18	10	-	-	77	15	8	-	-
Pulses dry	55	26	16	3	-	54	31	8	7	-	53	21	16	10	-	59	17	13	11	-
Pulses canned	72	16	9	3	-	76	13	7	4	-	73	17	5	5	-	68	25	4	3	-
Savoy cabbage	83	14	3	-	-	84	12	4	-	-	80	13	6	-	-	83	12	5	-	-
Soy germs	98	2	-	-	-	99	1	-	-	-	99	1	-	-	-	99	1	-	-	-
Spinach	69	23	8	-	-	69	27	4	-	-	74	20	6	-	-	85	8	7	-	-
Tomatoes	27	39	27	7	-	37	31	19	13	-	27	30	29	14	-	27	36	26	11	-
Zucchini	57	20	15	8	-	62	20	11	7	-	67	17	12	4	-	67	11	14	8	-
Beverages																				
Spirits	97	3	-	-	-	99	1	-	-	-	86	12	2	-	-	91	9	0	-	-
Beer	76	23	1	-	-	74	24	2	-	-	53	37	10	-	-	75	17	8	-	- **a**
Coffee	24	36	31	9	-	23	37	32	8	-	26	34	30	10	-	27	33	29	11	-
Sweet beverages	97	2	1	-	-	94	5	1	-	-	93	4	3	-	-	91	6	3	-	-
Tea	73	14	12	1	-	72	15	12	1	-	70	17	12	1	-	71	16	12	1	-
Water	3	32	40	25	-	2	33	39	26	-	2	35	37	26	-	3	31	41	25	-
Wine white	86	12	2	-	-	86	13	1	-	-	81	13	6	-	-	90	7	3	-	-
Wine red	61	19	15	5	-	73	19	3	5	- **a**	20	17	29	34	-	45	20	16	19	- **a**
Meat, processed meat, and fish																				
White meat	26	28	35	8	3	12	36	32	12	8 **a**	25	28	34	9	4	28	23	29	11	9
Red meat	69	22	9	-	-	80	12	8	-	-	74	13	13	-	-	77	16	7	-	-
Salami	48	17	20	5	10	54	13	16	9	8	38	13	21	9	19	37	29	17	8	8 **a**

Offal	93	2	5	-	-	95	1	4	-	-	89	6	5	-	-	95	0	5	-	- **a**
Bacon	76	15	9	-	-	79	15	6	-	-	75	15	10	-	-	74	16	10	-	-
Ham	38	33	27	2	-	45	32	21	1	-	41	27	28	4	-	37	28	29	5	-
Speck	95	3	1	-	-	92	6	2	-	-	86	10	4	-	-	89	8	3	-	-
Fish	29	59	11	1	-	35	52	12	1	-	31	52	12	5	-	27	60	11	2	-
Canned tuna	76	17	6	1	-	79	15	6	0	-	81	12	4	3	-	67	17	9	7	- **a**
Dairy products																				
Milk	38	17	14	8	-	51	11	8	25	5	54	10	8	22	5	60	19	8	13	0 **a**
Cheese	32	35	21	12	-	31	43	13	13	-	26	29	27	18	-	36	27	17	20	-
Ice cream	64	15	12	9	-	62	12	11	15	-	68	11	11	10	-	57	13	15	15	-
Mozzarella	39	23	28	10	-	36	25	25	14	-	41	22	27	10	-	41	19	28	12	-
Ricotta cheese	60	17	14	9	-	62	18	14	6	-	57	22	13	8	-	63	15	14	8	-
Yogurt	68	18	14	-	-	71	17	12	-	-	80	9	11	-	-	83	8	9	-	-
Eggs	40	47	12	1	-	45	43	11	1	-	38	43	17	2	-	40	44	15	1	-
Dressing																				
Butter	93	7	-	-	-	96	4	-	-	-	94	5	1	-	-	92	8	0	-	-
Mayonnaise	89	7	4	-	-	84	12	4	-	-	88	10	23	-	-	91	8	1	-	-
Margarine	96	4	-	-	-	96	4	-	-	-	99	1	-	-	-	98	2	-	-	-
Olive oil	40	43	17	-	-	35	51	13	-	-	36	51	13	-	-	48	30	21	-	-
Desserts																				
Homemade jam	81	9	10	-	-	80	4	14	-	-	78	9	13	-	-	79	10	11	-	-
Honey	85	7	8	-	-	84	6	10	-	-	85	6	9	-	-	86	5	5	-	-
Chocolate	62	29	9	-	-	63	28	9	-	-	64	27	9	-	-	82	8	10	-	- **a**
Cake	35	31	28	6	-	37	29	29	5	-	36	30	27	7	-	35	30	29	6	-
Other foods miscellanea and water																				
Sweeteners	83	8	2	7	-	80	6	4	10	-	82	9	3	6	-	81	10	4	5	-
Salt	13	46	16	21	4	14	45	18	17	6	12	47	16	20	5	13	47	15	20	5
Sugar (added)	31	15	42	11	-	40	27	30	13	-	30	16	40	14	-	35	18	27	20	-

a = Nominal Logistic Fit p < 0.05 Controls Vs MetS; see Table 5 for the average values

Table 7. Likelyhood ratio test for genders: foods within the observed range (whole model test)

Females		Males	
variable increase	pertinence to	variable increase	pertinence to
Water	MetS	Carrot	Controls
Alcohol	Controls	Chicory	MetS
Butter	Controls	Chocolate [a]	Controls
Coffee	MetS	Dried fruit	MetS
Crackers	MetS	Fennels	MetS
Fruit syrup	MetS	Fruit of the season	MetS
Fruit of the season	MetS	Garlic [a]	Controls
Ham	Controls	Ham	MetS
Homemade jam	MetS	Homemade jam	MetS
Homemade sandwich	Controls	Ice cream	MetS
Homemade fruit juice	MetS	Milk [a]	Controls
Lettuce	Controls	Pasta	MetS
Mayonnaise	MetS	Red Wine [a]	Controls
Potato	Controls	Sweeteners	MetS
Onions	Controls	White wine	Controls
White meat [a]	Mets	Yogurt	Controls
		Zucchini	MetS
		Pinapple	MetS

[a] = foods that were shown to be significantly different comparing the control Vs MetS if tested separately

The combination of foods that can be characteristic of MetS and Controls were reported according to the Likelihood Ratio Test (Table 7).

It is evident that considering the combination of foods, a very different picture is coming out, such that only two foods (fruit of the season and homemade Jam) are common for the two sexes and all the other are different and a more complex figure seems to takes shape in the development of the MetS or to maintain the control condition. Some aspects are very difficult to explain as for example the increase of the fruit of the season that turns out to increase the possibility of MetS in both sexes, whereas in the single item analysis a non-significant higher intake was found in females only.

Discussion

Some limitations are present in this research concerning first of all the enrollment, since a selection was operated by the doctors asking their patients with MetS to participate matching them subjects of the same age. This means that only subjects interested to the relationship between food and MetS were participating to the study.

The second weak point concerns the foods tested because they were representing about 90% of the total amount of the weekly caloric intake, and the lowest percentages were represented in the two groups suffering from MetS. This means that theoretically about 10% of the foods not included in the analysis could be partially responsible of MetS.

Another limitation can be determined by the lack of evaluation of micronutrients that are considered to counteract MetS [20,21].

However, the micronutrients that were not part of the analysis were in relation only to the about 10% of foods not considered in the analysis and should not influence critically the comparison between groups.

In general, the subjects participating to this study were those that the family doctor has to take care off in the daily practice and most of Control cases could not considered belonging to a healthy population.

Furthermore, it was not possible to compare the data of the three countries because the relative numbers were not enough to compare the two groups of subjects.

A part of these limitations some interesting indications can be drawn from the study.

The first observation which was common for both, female and males suffering from MetS, was a more consistent caloric intake. Compared to the values calculated with MSJ algorithm the caloric intake in MetS subjects was respectively >9.5 % in females and >4.7 % in males. Despite not excessive, at long term these increases may be determinant for the development of the disease.

The age of the two groups was < 52 years and one may not speculate about the incidence of MetS in relation to age since the subjects were selected by the family doctors. Because of this the incidence of the disease in the present study are higher than what has been determined in a previous survey conducted in some Italian towns where the incidence in a population between 35 and 65 years was < 20 % of the cases [16].

Foods were found to have a different impact in relation to the gender, and this could mean that the epidemiological studies should consider these aspects in long term survey and also the need of different treatment in terms of drugs.

The reason of this difference between genders is unknown and probably belongs to the hormonal balance. This hypothesis may arise also by the evidence that the intake of white meat was more consistent in females with MetS. The quite common practice (although is prohibited) to give estrogens to reduce the aggression of chickens and turkey in breeding farm may be one of the causes. Meat deriving from these animals is a substantial part of the white meat intake in Italy.

Some data that are considered common determinants of MetS, such as the excessive intake of carbohydrates, is not emerging from this study. At the opposite the total amount of carbohydrate-based food (consisting of about 80 % of the weight in carbohydrates) were respectively 1366 g in the normal females and 1203 g in females with MetS, the same was for males consisting of 1606 g/week for controls and 1499 g/week for MetS.

The amount of calories from fats were similar in all the groups (difference < 2 %) and also the ratio between carbohydrates or soluble sugars and fats was not having a discriminant power to differentiate MetS.

Some author found that carbohydrate restriction has a more favorable impact on the disease than low fat diet and our results do not confirm these findings [22]. Furthermore, our data do not confirm the negative impact of soluble sugars as other author have shown to be associated with MetS in females [23].

In terms of processed meat, it was shown that salami intake was lower in the MetS group and also the offal intake.

This may indicate more prudence in defining the processed meat as "carcinogenic to humans" [24].

A part of the quantity of processed meat intake, a quite careful distinction should be made about the way of producing this type of food which in many cases do not contain nitrates (or minimal amount), particularly when they are produced directly by the consumers like in some rural community.

The red wine seems to be protective in males, at least in the amount used in this study as average 610 mL/week in the Control group and 415 mL /week in the MetS group, that at the end was less than one alcoholic unit/day for both groups.

Other foods such as garlic and chocolate seem to be protective in males (not in females) and one may speculate the presence of powerful antioxidants in both [25,26].

One particular food, canned tuna, was found significantly more used in MetS males. Fish and fish oil are giving conflictual results on the disease, but recently were considered healthy for some author [27]. In our study we could not show any favorable activity of these foods. This is an example on how the food quantities, the context of a diet, the country, down to the single community may be determinant for the disease. All these aspect makes more complex the pathogenesis of MetS which also belongs to the genetics and epigenetics traits together with the microbiota.

Once the foods were analyzed together, a quite different picture was emerging where the interactions take place and single elements are diluted or amplified such that even drinking water may have a role (in females only), and genders differences are becoming extremely evident. Among the 17 foods for females and 18 foods for males which are bound respectively to the Controls or MetS conditions, only two are common: fruit of the season and homemade jam whose increasing intake was found related to the MetS.

Al the other foods are different, no matter if the Increased quantities are bound to MetS or Controls.

One further important aspect arising from this study has to be mentioned and concerns the concomitant diseases. It was clear that people suffering from MetS have to be treated with more drugs. Considering the costs in terms of drug expenses- which in Italy is covered mostly by the Government- for an average life expectancy of 25 years more (from about 50 years up to about 75) the estimated cost is > € 20,000/subject.

This means that will be much more convenient to use this money for prevention and education to give more life to the years.

Conclusions

In the context of a Mediterranean diet and in our experimental conditions it seems that MetS both in females and males was determined by higher amount of caloric intake, without a clear distinction between carbohydrates, fats, fibers, proteins and alcohol. Concomitant diseases such as CVD and osteoarthritis (in males only) were more common indicating a fragile healthy condition in subjects suffering from MetS.

A part of the caloric intake, the pattern of foods bound to the MetS was found completely different in females and males.

Some particular foods were more common in MetS, such as white meat (in females) or seasonal fruits and homemade fruit juice (for both genders). In males, the processed meat and red wine intake -in the relative limited quantities that have been determined - were found to be protective.

However, once the different foods were analyzed together a completely different relationship with MetS emerged, indicating that a single food category cannot be considered the cause of the disease which seems to be determined by the interactions of many foods, that again are different for females and males.

The disease has a heavy social and economic impact and despite common diagnostic aspects the causes and the remedies of MetS in terms of foods have such a proteiform aspect that any community (country, town, village) could have peculiar way to face it.

Larger epidemiological studies in each territorial context with specific food pattern are needed to give appropriate information on healthy foods. These aspects belong to the social/educational area and can be faced only with the help of the Governments, family doctors and local Municipalities.

Acknowledgements

The study was supported largely by private funding and no competing interest have to be declared. The Bracco Spa- Milan Italy was partially supporting this study with a grant of € 100,000.

The authors are grateful to the Municipalities of Rende, Rovito and San Lucido which made the surgeries available.

Contribution

UC was preparing the protocol, visited all the subjects and wrote the article; GC visited all the subjects and was charged for the FIA; GM was charged with the ultrasound analysis; MR was assisting in the logistic of the investigation; OV was taking care of data input; MR was making all the statistical calculations using JMP Pro 14.1 software of SAS institute Inc.

References

1. Eckel SM, Alberti KG, Grundy SM (2010) The metabolic syndrome. *Lancet* 375: 181-183.
2. O'Neil S, O'Driscoll L (2015) Metabolic syndrome: a closer look at the growing epidemic and its associated pathologies. *Obesity rev* 16: 1-12. [Crossref]
3. Samson SL, Gaber AJ (2014) Metabolic syndrome. *Endocrinol Metab Clin North Am* 43: 1-23.
4. Bellia A, Giardina E, Lauro D (2009) The Linosa study: epidemiological and heritability data of the metabolic syndrome in a Caucasian genetic isolate. *Nutr Metab Cardiovasc Dis* 19: 455-461. [Crossref]
5. Kissebah AH, Sonnenberg GE, Myclebust J (2000) Quantitative trait loci in chromosomes 3 and 17 influence phenotypes of the metabolic syndrome. *Proc Natl Acad Sci USA* 97: 14478-14483. [Crossref]
6. Loss RJ, KattamarzyK PT, Rao DC (2003) Genome-wide linkage scan for the metabolic syndrome in the HERITAGE Family Study. *J Clin Endocrinol Metabol* 88: 5935-5943. [Crossref]
7. Edwards KL, Hutter CM, Wan JY (2008) Genome-wide linkage scan for metabolic syndrome: the GENNID study. *Obesity (Silver Spring)* 16: 1596-1601. [Crossref]
8. Fryling TM, Timpson M, Weedon MN (2007) A common variant in the FTO gene is associated with body mass index and predispones to childhood and adult obesity. *Science* 316: 889-894. [Crossref]
9. Torres S, Fabersani E, Marquez A (2018) Adipose tissue inflammation and metabolic syndrome. The proactive role of probiotics. *Eur J Nutr.* [Crossref]
10. Festi D, Schiumerini R, Eusebi LH (2014) Gut microbiota and metabolic syndrome. *World J Gastroenterol* 20: 16079-16094. [Crossref]
11. Kaur JA (2014) Comprehensive review on metabolic syndrome. *Cardiol Res Pract* 2014: 941162. [Crossref]
12. Ludwig DS (2018) Dietary carbohydrates: role of quality and quantity in chronic disease. *BMJ* [Crossref]
13. Yamaoka K, Tango T (2012) Effects of lifestyle modification on metabolic syndrome: a systematic review and metanalysis. *BMC Med* 10: 138. [Crossref]
14. Kastorini CM, Milions HJ, Esposito K (2011) The effect of Mediterranean diet on metabolic syndrome and its component. *J Am Coll Cardiology* 57: 1299-1313. [Crossref]
15. Babio N, Toledo E, Estruch R (2014) Mediterranean diets and metabolic syndrome status in the PREDIMED randomized trial. *CMAJ* 186: E649-E657. [Crossref]
16. Cornelli U, Milani L, Perra A (2006) The use of polyglucosamine in the metabolic syndrome control. *Med Biol* 4: 45-54.
17. Cornelli U, Belcaro G, Recchia M, D'Orazio N (2017) Long-term treatment of overweight and obesity with polyglucosamine (PG L112): randomized study compared with placebo in subjects after caloric restriction. *Curr Dev Nutr.* [Crossref]
18. Belcaro G, Nicolaides AN, Laurora G (1996) Ultrasound morphology classification of the arterial wall and cardiovascular events in a 6-year follow-up study. *Arterioscl Thromb Vasc Biol* 16: 851-856. [Crossref]
19. Lesaffre E, Albert A (1989) Multiple group logistic regression diagnostic. *Appl Stat* 38: 425-440.
20. Goncalves A, Amiot MJ (2017) Fat-soluble micronutrients and metabolic syndrome. *Curr Opin Clin Nutr Metab care* 26: 492-497. [Crossref]
21.
22. Dakshinamurti K (2015) Vitamins and their derivatives in the prevention and treatment of metabolic syndrome disease (diabetes). *Can J Physiol Pharmacol* 93: 355-362. [Crossref]
23. Volek JS, Phinney SD, Forsythe CE (2009) Carbohydrate restriction has more favorable impact on the metabolic syndrome than low fat diet. *Lipids* 44: 297-309. [Crossref]
24. Song S, Lee JE, Song WO (2014) Carbohydrate intake and refined-grain consumption are associated with metabolic syndrome in the Korean adult population. *J Acad Nutr Diet* 114: 54-62. [Crossref]
25. Bouvard V (2015) IARC Carcinogenicity of consumption of red and processed meat. *Lancet oncology* 16: 1599-1600. [Crossref]
26. Banerjee SK, Mukherjee PK, Maulik SK (2013) Garlic as an antioxidant: the good, the bad and the ugly. *Physiother Res* 17: 97-106. [Crossref]
27. Serafini M, Bugianesi R, Maiani G (2003) Plasma antioxidant from chocolate. *Nature* 424: 10-13. [Crossref]
28. Karlsson T, Rosendahl-Riise H,Dierkes J (2017) Association between fish intake and the metabolic syndrome and its component among middle-aged men and women: the Horderland Healthy Study. *Food Nutr Res* 61: 1347-1479. [Crossref]