



Are Glycemic Index and Glycemic Load associated with risk of cutaneous melanoma? A case-control study in an Italian population.

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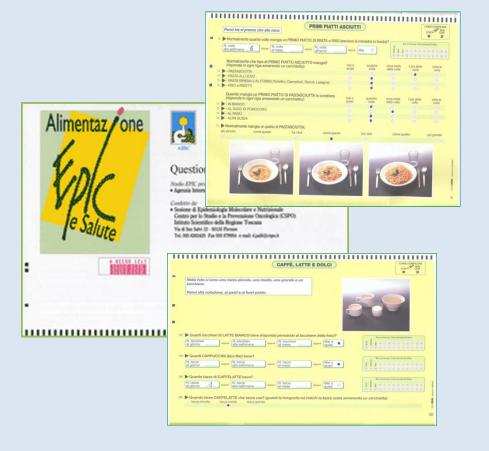
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Background

Several lines of evidence suggest a potential role of glucose and insulin in increasing risk of cancer at several common sites and promoting tumor growth (1). For these reasons, it has been suggested that the nature of the carbohydrates consumed may play a role in carcinogenesis. Meta-analyses on Glicemic Index (GI), Glicemic Load (GL) and cancer risk have been recently made available on selected cancer sites. The National Enhanced Cancer Surveillance study (2) suggested diets high in GI and GL may be associated with an increased risk of selected digestive tract and prostate cancers. Findings from the European Prospective Investigation in Cancer and Nutrition (EPIC) cohort on breast cancer (3) suggested that GL and carbohydrate intake are positively associated with estrogen and progesterone receptor tumors among postmenopausal women. The present study was designed to address the possibility that GI and GL may influence the risk of cutaneous melanoma in a northern Italy community, using a population-based case-control design.

Methods All patients diagnosed with cutaneous melanoma in the years 2005-2006 in five provinces of the Emilia Romagna region (northern Italy) were recruited at the Dermatologic Units of these provinces. The cases were matched according to sex, age and province of residence with population controls drawn from the National Health Service Emilia-Romagna directory. Each study participant compiled a food frequencies questionnaire specifically developed within the European Prospective Investigation into Cancer and Nutrition (EPIC) study for the Northern Italy population. The EPIC questionnaire was designed to capture habitual diet/eating behaviors during the past 12 months. Participants were asked to respond to 248 questions about 188 different food items, including seasonal foodstuffs, and to indicate the number of times a given item was consumed (per day, week, month, or year), from which the absolute frequency of consumption of each item was calculated. Average dietary GI and GL were then calculated for each subject, and GI of food items containing carbohydrates was obtained from the Italian Glycemic Index Table.

Figure 1. Epic Food Frequency Questionaire



stratified analysis.

Figure 2. Provinces included in the study



Table 3. Crude and adjusted Odds ratios (95% confidence interval) for melanoma according to Glycemic Load and Glycemic Index in sex-

Quintiles

		·	Quillule	S					
	Q1	Q2	Q3	Q4	Q5	P-trend ^l			
Glycemic Load									
Men									
Cases/controls	41/78	34/75	33/55	31/54	36/57				
OR^1	1.00	0.90 (0.53-1.53)	1.13 (0.63-2.04)	1.20 (0.67-2.15)	1.11 (0.64-1.93)	0.485			
OR^2	1.00	0.82 (0.47-1.42)	1.07 (0.58-1.97)	1.05 (0.57-1.93)	0.86 (0.47-1.57)	0.808			
Women									
Cases/ controls	20/66	35/69	43/89	49/90	58/86				
OR^1	1.00	1.88 (0.96-3.66)	1.67 (0.88-3.14)	1.91 (1.02-3.59)	2.38 (1.25-4.52)	0.070			
OR^2	1.00	2.08 (1.04-4.14)	` '	1.91 (0.99-3.66)	` '	0.111			
Glycemic Index									
Men									
Cases/ controls	34/72	32/62	36/65	35/64	38/56				
OR^1	1.00	1.03 (0.56-1.92)	1.02 (0.57-1.84)	1.16 (0.64-2.10)	1.31 (0.70-2.47)	0.493			
OR^2	1.00	1.02 (0.54-1.93)	0.91 (0.50-1.66)	1.02 (0.56-1.88)	1.11 (0.58-2.14)	0.967			
Women									
Cases/controls	37/72	36/82	38/79	45/80	49/87				
OR^1	1.00	0.81 (0.46-1.41)	0.92 (0.53-1.61)	1.00 (0.57-1.75)	1.06 (0.62-1.84)	0.154			
OR^2	1.00	0.79 (0.45-1.40)	0.86 (0.491.51)	0.93 (0.531.65)	0.88 (0.49-1.56)	0.428			

¹Unadjusted analysis

²Adjusted for saturated fats, vitamin D, fiber, total energy intake, phototype, skin sensitivity to sun exposure, sunburns history, BMI and education

	Cases		Cor	Controls	
	$\frac{1}{N}$			(%)	
Subjects	380	(34.6)	n 719	(65.4)	
Gender	300	(31.0)	(1)	(03.1)	
Male	175	(46.1)	319	(44.4)	
Female		(53.9)	400	(55.6)	
Age (years)	203	(33.7)	400	(33.0)	
<40	108	(15.0)	64	(13.0)	
40-59		(42.5)	170	(34.4)	
60-79		(38.7)	235	(47.6)	
>80	27	(3.8)	25	(5.6)	
Education	21	(3.0)	25	(3.0)	
Elementary or less	91	(23.9)	170	(23.6)	
Middle school	95	(25.0)	176	(24.5)	
High school	136	(35.8)	266	(37.0)	
College or more	54	(15.3)	107	(14.9)	
Marital Status	J4	(13.3)	107	(14.7)	
Married	257	(67.6)	493	(68.7)	
Unmarried/single	68	(17.9)	103	(08.7) (14.3)	
Divorced	23	(6.0)	48	· /	
		` ′		(6.6)	
Widowed	31	(8.2)	74	(10.3)	
Unknown	1	(0.3)	1	(0.1)	
BMI (kg/m ²)	21	(9.2)	15	((2)	
<18.5	31	(8.2)	45	(6.3)	
$\geq 18.5 \text{ to } < 25$		(43.2)	306	(42.7)	
\geq 25 to <30		(35.0)	287	(39.9)	
≥30	52	(13.6)	81	(11.3)	
Phototype	105	(27.6)	100	(15.2)	
I		(27.6)	109	(15.2)	
II		(35.8)	238	(33.1)	
III		(32.1)	312	(43.4)	
IV	17	(4.5)	60	(8.3)	
Sunburn history	100	(47.0)	450	((2,0)	
Never		(47.9)	452	(62.9)	
Before 18 y		(28.4)	164	(22.8)	
After 18 y	90	(23.7)	103	(14.3)	
Skin sun reaction (speed					
to tan and tendency to					
burn)					
High tendency to	21	(5.5)	22	(3.1)	
burn and never tan					
High tendency to	44-	(20.0)	101	(10.2)	
burn and moderate	117	(30.8)	131	(18.2)	
tan					
Moderate tendency	4	(12.1)	0	(40.7)	
to burn and gradual	160	(42.1)	357	(49.7)	
tan					
No tendency to burn	65	(17.1)	149	(20.7)	
and golden tan		(=)	,	(= 0.1.)	
No tendency to burn	17	(4.5)	60	(8.3)	
and intense tan	11	(1.5)	00	(0.5)	

 Table 1. Characteristics of study subjects

Results

Three hundred and eighty cases (175 men and 205 women, aged 58 ± 16 and 53 ± 15 years, respectively) and 719 age-, sex- and province of residence-matched referents were finally included in the analysis. Descriptive characteristics of study population are reported in our Table 1. Cases tended to have more fair skin types, high tendency to burn and were more likely to report a history of sunburns (chi-square Pvalues <0.000). GI, GL and other dietary carbohydrates (total carbohydrates, total sugars, starch and fiber) were adjusted for total energy intake using the nutrient residual method as described by Willett (4). GI and GL were positively correlated (r=0.44, 95%CI 0.39-0.48). A positive association between GL, GI and melanoma risk emerged in the comparison between highest (Q5) and lowest (Q1) quintiles in the crude model, OR=1.53 (95%CI 1.02-2.30) and 1.16 (0.77-1.76) respectively but remained in the adjusted model (for saturated fats, fiber, vitamin C, vitamin D, energy intake, phototype, skin sensitivity to sun exposure, sunburns history, BMI and education) only for GL, OR=1.35 (0.80-2.27) (Table 2). Gender-specific analysis showed that the association between GL and melanoma risk was restricted to females, being entirely absent in males (Table 3). The association between GL and disease risk in females was not linked to a specific age group (OR in subjects <50 =2.29, 95% CI 0.61-8.62) and in the oldest age category (OR=2.96, 95% CI 0.96-9.13). Plots estimating the relation between the odds of being a case and GI and GL values, produced using regression spline analysis, appear to confirm a direct relation between GL – but not GI – with melanoma risk in females (Figure 3).

Table 2. Crude and adjusted Odds ratios (95% confidence interval) for melanoma according to Glycemic Load and Glycemic Index.

All			Quintiles						
subjects	$Q1^5$	Q2	Q3	Q4	Q5	P-trend			
	Glycemic Load								
Cases/controls	61/ 144	69/144	76/144	80/144	94/143				
Median	92.0	112.9	122.0	132.1	149.7				
OR^1	1.00	1.19 (0.79-1.80)	1.28 (0.84-1.95)	1.40 (0.93-2.12)	1.53 (1.02-2.30)	0.074			
OR^2	1.00	1.16 (0.74-1.83)	1.26 (0.78-2.02)	1.28 (0.79-2.07)	1.35 (0.80-2.27)	0.450			
	Glycemic Index								
Cases/controls	71/ 144	68/144	74/144	80/144	87/144				
Median	47.7	50.1	51.7	53.2	55.7				
OR^1	1.00	0.90 (0.60-1.36)	0.97 (0.65-1.45)	1.08 (0.72-1.62)	1.16 (0.77-1.76)	0.127			
OR^2	1.00	0.78 (0.51-1.22)	0.85 (0.55-1.31)	0.88(0.56-1.37)	0.88 (0.55-1.42)	0.802			

¹Unadjusted analysis

²Adjusted for saturated fats, vitamin C, vitamin D, fiber, total energy intake, phototype, skin sensitivity to sun exposure, sunburns history, BMI and education

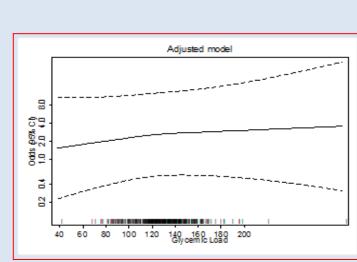
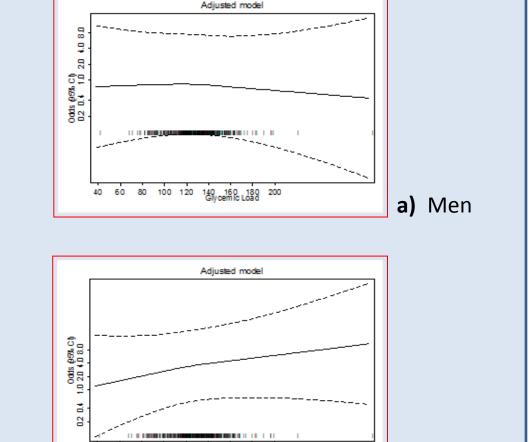


Figure 3. Restricted cubic spline regression analysis of the odds of being a case according to score of the Glycemic Index and Glycemic Load



Conclusion

Our analysis conducted on quintile showed a clear association between melanoma risk and GL while the role of GI was unstable. Indeed multivariate analyzes adjusted for major confounding factors showed RR melanoma increased in relation to GL increase, assuming a possible association between melanoma risk and this index. This association is evident in the whole population for crude and for adjustment analysis. Stratifying the analyses by gender the risk of melanoma seems confined to women even if we divide the sample for age confirming both a significant interaction between sex and food consumption. Our data partially support our hypothesis that dietary glycemic index and glycemic load are positively associated with melanoma. Indeed we only found a marginally significant association between melanoma risk and increasing quintiles of GL in crude and adjusted analysis of women population. However further prospective studies on larger population are required to clarify and validate this association.

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b) Women