Low-Risk Diet for Breast Cancer in Italy

Silvia Franceschi, Carlo La Vecchia, Antonio Russo, Eva Negri, Adriano Favero, and Adriano Decarli

Servizio di Epidemiologia, Centro di Riferimento Oncologico, 33081 Aviano (PN), Italy. Phone: 39-434-659232; Fax: 39-434-659222.

Abstract
To define a low-risk diet for breast cancer in Italy, a multicentric case-control study of 2569 incident cases of breast cancer and 2588 controls from Italy was analyzed. A logistic regression model was applied to the estimated intake of five macronutrients and used to compute a diet-related risk score (RS). The pattern of macronutrient and food group intake across RS deciles was defined. The mean of diet-related RSs across subsequent risk deciles ranged from 0.83 to 1.44. Total energy intake first decreased slightly, from the first to the second decile, and then increased, mostly in the last three risk deciles. Intake of starch increased in absolute and relative terms, whereas saturated fat intake rose in absolute terms but remained stable as a proportion. A relative decline was observed for unsaturated fat and sugars, with a hint, however, of U-shape effect. From a food group viewpoint, there was a marked increase in the intake of bread and cereal dishes, cakes and desserts, and refined sugar across subsequent deciles, whereas the consumption of vegetables, olive and seed oils, and fruit decreased.

Introduction
Breast cancer rates have been relatively low in Mediterranean countries as compared to most other Western ones (1). The traditional Mediterranean diet is relatively rich in carbohydrates, vegetables, and fruits, but the total fat intake, in proportional terms, is not particularly low. Olive oil, however, predominates among seasoning fats (2). Studies of the relationship between diet and breast cancer have been focused thus far on defining the specific role of various food groups, macronutrients (chiefly fat), and micronutrients (3). In a large case-control investigation from six different Italian areas, from which this report derives, breast cancer risk was positively associated with the intake of bread and cereal dishes, pork and processed meats, and refined sugar (4). Conversely, intakes of milk, poultry, fish, potatoes, and raw vegetables were negatively associated with risk (4). Oils and fats did not increase cancer risk, whereas olive oil and selected seed oils seemed to provide some protection (5). Among major energy sources, high starch intake was associated with an increased risk, whereas monounsaturated and polyunsaturated fats were associated with a decreased risk (6). High intake of several micronutrients, particularly β-carotene, vitamin E, and calcium, seemed protective against breast cancer (7). These findings are in agreement with other investigations from Southern Europe (8, 9).

Rarely have multivariate approaches been used to identify low-risk dietary patterns (10). Preventive strategies, however, would benefit from understanding the overall dietary pattern, which could reduce breast cancer occurrence. It is therefore of interest to identify, in terms of macronutrients and food sources, the type of diet related to the lowest breast cancer risk.

Materials and Methods
Data were derived from a case-control study of breast cancer, carried out in six Italian geographical areas, whose design and methods have been described elsewhere (4–7). Briefly, cases were 2569 women with incident histologically confirmed breast cancer, ages 23–74 years (median age, 55 years). Controls were 2588 women, ages 20–74 years (median age, 56 years), hospitalized for acute, nonneoplastic, non-hormone-related conditions (i.e., 22% traumas, 33% other orthopedic diseases, 15% acute surgical conditions, 18% eye diseases, and 12% other miscellaneous diseases). Between 1991 and 1994, trained interviewers administered a validated food frequency questionnaire (11, 12) including questions on 78 foods and recipes grouped into six sections and specific questions on individual fat intake pattern. Italian food composition tables, appropriately checked and supplemented with other published data (13), and information from the manufacturers were used to estimate the intake of selected nutrients.

Food items and recipes were grouped into 16 food groups: milk; bread and cereal dishes; soups; eggs; poultry; red meat; pork and processed meat; fish; cheese; raw vegetables; cooked vegetables; potatoes; citrus fruits; other fruits; cakes and desserts; and refined sugar. For each subject, the weekly frequency of intake of each food group was computed and translated into grams/day by multiplying the intake frequency by individual portion size. For refined sugar, it corresponded to four teaspoons. Estimates of intake in grams of olive oil, seed oils, and butter used as a condiment were derived from the frequency and self-assessed quantity of use as well as from estimates of fat included in various foods and recipes (4–6).

Data Analysis. We fitted a multiple logistic regression equation that included terms for age in quinquennia, center, major correlates of breast cancer risk in our study (i.e., years of education, parity, menopausal status, and quintile of alcohol consumption), and five macronutrients (starch, sugar, protein, saturated fat, unsaturated fat).
The abbreviation used is: RS, risk score.

Fig. 1. Total energy and proportional intake of five macronutrients by decile of breast cancer diet-related RS (Italy, 1991–1994).

Table 1 Intake of macronutrients and food groups (in grams) by decile of breast cancer diet-related RS (Italy, 1991–1994)

<table>
<thead>
<tr>
<th>Macronutrient or food group</th>
<th>Mean daily intake (g)</th>
<th>Decile of breast cancer diet-related risk score</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Starch</td>
<td>107</td>
<td>114</td>
</tr>
<tr>
<td>Sugars</td>
<td>116</td>
<td>98</td>
</tr>
<tr>
<td>Protein</td>
<td>90</td>
<td>83</td>
</tr>
<tr>
<td>Saturated fat</td>
<td>25</td>
<td>24</td>
</tr>
<tr>
<td>Unsaturated fat</td>
<td>46</td>
<td>39</td>
</tr>
<tr>
<td>Bread and cereal dishes</td>
<td>124</td>
<td>134</td>
</tr>
<tr>
<td>Soups</td>
<td>73</td>
<td>75</td>
</tr>
<tr>
<td>Eggs</td>
<td>13</td>
<td>13</td>
</tr>
<tr>
<td>Poultry</td>
<td>72</td>
<td>57</td>
</tr>
<tr>
<td>Red meat</td>
<td>77</td>
<td>69</td>
</tr>
<tr>
<td>Pork and processed meat</td>
<td>27</td>
<td>25</td>
</tr>
<tr>
<td>Fish</td>
<td>45</td>
<td>38</td>
</tr>
<tr>
<td>Cheese</td>
<td>44</td>
<td>46</td>
</tr>
<tr>
<td>Milk</td>
<td>218</td>
<td>185</td>
</tr>
<tr>
<td>Raw vegetables</td>
<td>196</td>
<td>162</td>
</tr>
<tr>
<td>Cooked vegetables</td>
<td>132</td>
<td>114</td>
</tr>
<tr>
<td>Potatoes</td>
<td>39</td>
<td>40</td>
</tr>
<tr>
<td>Citrus fruits</td>
<td>137</td>
<td>120</td>
</tr>
<tr>
<td>Other fruits</td>
<td>421</td>
<td>330</td>
</tr>
<tr>
<td>Cakes and desserts</td>
<td>39</td>
<td>36</td>
</tr>
<tr>
<td>Refined sugar</td>
<td>90</td>
<td>80</td>
</tr>
</tbody>
</table>

saturated fat, and unsaturated fat; Ref. 14). Unsaturated fats were computed by adding polysaturated fat and monounsaturated fat. For each woman (i; case or control), a diet-related RS3 (RS3) was defined by disentangling estimated parameters for each macronutrient, i, from the logistic equation as follows:

$$RS = \exp \left( \sum_{i=1}^{S} b_iZ_i \right)$$  \hspace{1cm} (1)

where $Z_i$ is the intake (in kcal) and $b_i$ is the regression coefficient of macronutrient $i$ for woman $j$. Women were then classified by decile of RS distribution of cases and controls combined.

To validate our diet-related RS, we used the jackknife method (15, 16). Each subject was removed in turn from the dataset, and the logistic regression model was carried out on the remaining $(n - 1)$ subjects. The new set of logistic regression parameters was used to compute an independent RS for the subject left out of the dataset. A Pearson's correlation coefficient of 0.9994 was found between the RS we used and those derived from the jackknife method.

The mean composition of the diet of cases and controls combined was evaluated in each RS decile in terms of macronutrients, food groups, and types of fat used as a condiment.

Results

Fig. 1 gives total energy intake and the proportion of energy from starch, sugars, protein, and saturated and unsaturated fats, according to the decile of diet-related RS. RS ranged from 0.83 to 1.44. After a decline from the first to the second decile and a plateau at approximately 1800 kcal/day, total energy in-
increased in the last three deciles, most notably in the last risk decile, to 2515 kcal/day. Starch intake approximately doubled in both absolute (from 447 to 1003 kcal/day) and relative terms, from 24% of total energy in the RS lowest decile to 40% in the highest one. Saturated fat intake increased with increasing RS decile (from 228 to 297 kcal/day) but remained stable as a proportion (12%). A relative decline was seen from the lowest to the highest RS decile for sugars (from 23 to 17%) and unsaturated fats (from 22 to 15%). Thus, the lowest RS decile showed a specific pattern in which the intake of sugars and unsaturated fat predominated, accounting together for 45% of energy intake.

Table 1 gives the intake in grams/day of major macronutrients and food groups by RS decile. The absolute intake of starch and, to a lesser extent, saturated fat increased across subsequent risk deciles. The pattern was less clear for other macronutrients. Intakes of sugars and unsaturated fat showed a U-shaped distribution. There was an increase in bread and cereal dishes, cheese, cakes and desserts, and refined sugar across subsequent RS deciles, particularly in the last one. Conversely, the consumption of different types of vegetables and fruits tended to decrease substantially. Also poultry and fish consumption declined across RS deciles. Thus, the lowest risk decile was characterized by especially high intakes of vegetables and fruits. Risk patterns were similar in pre- and postmenopausal women (data not shown).

To further describe a low-risk diet, Fig. 2 gives the mean number of average servings/week for selected food groups by decile of dietary-related RS. Women with a RS below 1.00 tended to eat fruits and vegetables more or equally often than bread and cereal dishes. In the highest RS deciles, and again, especially in the last one, a rise in the consumption of bread and cereal dishes, cakes and desserts, and refined sugar was evident.

Fig. 3 shows daily intake of different types of fat as a condiment. The intake of olive oil and seed oils fell substantially, whereas butter consumption rose slightly across subsequent RS deciles.

Discussion
The presented approach attempts to provide new insights on the relationship between dietary habits and breast cancer risk, with special reference to a Mediterranean population. It goes beyond reliance on odds ratios for specific dietary components (4–7), allowing a combined evaluation of the influence of nutrients and food sources. Because of the persisting ignorance on cancer mechanisms, vegetable and fruit intake was preferred to micronutrient intake as an indicator of the intake of potentially beneficial compounds.

It is clear that an increase in total energy intake is a component of the three highest RS deciles, most notably of the last one, whereas no material difference was observed between the second and seventh decile. The predominance of starch and hence bread and cereal dishes (i.e., more than 80% of starch...
intake in study women) increased appreciably across subsequent RS deciles. In a population such as the Italian one, in which refined cereals, virtually all from wheat, are consumed, high starch intake is an indicator of a diet rich in energy but potentially poor in beneficial micronutrients (4, 7). Increased intakes of cakes and desserts and refined sugar were other features of the highest risk deciles, chiefly of the last one. Interestingly, refined cereals as well as refined sugar can produce glycemic overload, compensatory increase of blood insulin, and, in the long term, insulin resistance (17). These conditions may lead to cellular growth promotion in the breast via specific hormones or growth factors (18).

Conversely, the intake of sugars, unsaturated fat, and, on the food side, fruits and vegetables declined across RS deciles. Saturated fat constituted the macronutrient whose intake, as a proportion of total energy intake, was the most stable (12%) across risk deciles. Still, women in the highest risk decile ate about a third more saturated fat than those in the lowest one. This is compatible with an adverse effect of saturated fat intake on breast cancer beyond a certain threshold, which may or may not be reached in a specific population (18).

The definition of a low-risk diet for breast cancer in terms of foods or food groups is of special relevance from a practical viewpoint. In the lowest-RS decile, women consumed 26 servings/week of fruits and 20 servings/week of vegetables. Servings of bread and cereal dishes were consumed somewhat less frequently, i.e., 16 servings/week. Conversely, 37 servings/week of bread and cereal dishes were reported by women in the highest risk decile, as compared to 18 servings/week of fruits and 13 servings/week of vegetables.

Olive oil was the chief source of unsaturated fat and markedly predominated among seasoning fats in the lowest risk deciles. Fruit intake, the major source of sugars in our population, showed a similar curve. However, after some plateau, the absolute intake of unsaturated fat and sugars increased again in the three highest risk deciles. Therefore, the specific effect of some macronutrients (e.g., sugars) may vary depending on their food sources (e.g., fruits in low-risk women, but refined sugar in high-risk ones).

The use of the same dataset to construct the diet-related RS and to evaluate the risk differentials associated with it is open to criticism. The low-risk diet presented here awaits confirmation from independent data from a similar Southern European population. Furthermore, because RS deciles were derived from the comparison of cases and controls, this study shares the strengths and limitations of hospital-based case-control studies (19). Although case recruitment was not population based, cases were identified in the major public hospitals of the area under surveillance, reducing the scope for selection bias. With reference to the control group, only acute conditions unrelated to known or likely risk factors for breast cancer or to dietary modifications were included. Furthermore, a separate comparison of cases with major diagnostic categories of controls produced mutually consistent results. Conversely, the hospital-based design kept refusals to a minimum and probably improved the comparability of diet recall by cases and controls. The food frequency questionnaire had been proven reproducible (11) and valid (12).

In conclusion, the presented model is easily transferable into preventive measures, because it points to an overall protective dietary pattern (chiefly, high vegetable and oil intake) that may help in reconciling some uncertainties and
discrepancies of previous studies (e.g., with respect to the role of fat; Ref. 20).

Acknowledgments

We thank Dr. Renato Talamini and Olinda Volpato for study coordination and Luigina Mei for editorial assistance.

References


Cancer Epidemiology, Biomarkers & Prevention

Low-risk diet for breast cancer in Italy.
S Franceschi, C La Vecchia, A Russo, et al.

Updated version
Access the most recent version of this article at:
http://cebp.aacrjournals.org/content/6/11/875

E-mail alerts
Sign up to receive free email-alerts related to this article or journal.

Reprints and Subscriptions
To order reprints of this article or to subscribe to the journal, contact the AACR Publications Department at pubs@aacr.org.

Permissions
To request permission to re-use all or part of this article, contact the AACR Publications Department at permissions@aacr.org.