ABSTRACT  The strongest evidence that monounsaturated fat may influence breast cancer risk comes from studies of southern European populations, in which intake of oleic acid sources, particularly olive oil, appears protective. No previous study has examined the relation of adipose tissue fatty acid content to breast cancer in such a population. We used adipose biopsies with diverse fat intake patterns gathered in 5 European centers, including southern Europe (Malaga, Spain), to test the hypothesis that stores of oleic acid or other monounsaturates are inversely associated with breast cancer. Gluteal fat aspirates were obtained from 291 postmenopausal incident breast cancer patients and 351 control subjects, frequency-matched for age and catchment area. Logistic regression was used to model breast cancer by monounsaturates, with established risk factors controlled for. Oleic acid showed a strong inverse association with breast cancer in the Spanish center. The odds ratio for the difference between 75th and 25th percentiles was 0.40 (95% CI: 0.28, 0.58) in Malaga and 1.27 (0.88, 1.85) in all other centers pooled, with a peak at 2.36 (1.01, 5.50) for Zeist. Palmitoleic and myristoleic acids showed evidence of an inverse association outside Spain, and cis-vaccenic acid showed a positive association in 3 centers. These data do not support the hypothesis that increasing tissue stores of oleic acid are protective against breast cancer in non-Spanish populations. This finding implies that the strong protective associations reported for olive oil intake in dietary studies may be due to some other protective components of the oil and not to the direct effect of oleic acid uptake. Alternative- ly, high olive oil intake may indicate some other protective aspect of the lifestyle of these women.  Am J Clin Nutr 1998;68:134–41.

KEY WORDS  Monounsaturated fat, oleic acid, fatty acids, breast cancer, adipose tissue, olive oil, EURAMIC Study, Europe

INTRODUCTION  Although many factors—genetic, reproductive, and others—have been linked to breast cancer risk, much of the variation in breast cancer risk across countries and cultures remains unexplained (1, 2). The great geographic variation in breast cancer rates has spurred interest in diet as a potential risk factor, leading to extensive research on fat intake. Recent studies indicate that monounsaturated fat consumption may play a role in breast cancer.

Dietary sources of monounsaturated fatty acids are varied. Most dietary monounsaturates are 16, 18, or 20 carbons in length. Palmitoleic acid (16:1n–7) is a general minor component (<2%) of animal and vegetable fats but is more abundant in fish and some nut oils. cis-Vaccenic acid (18:1n–7) is a minor component of most seed oils and a larger component of seafood. Oleic acid (18:1n–9) is a major monounsaturated fatty acid. Although olive oil is the richest dietary source of oleic acid, it is also a major component of most animal fats and makes up a sizable fraction of most vegetable oils. Both eicosenoic (20:1n–9) and erucic (22:1n–9) acids are found in small amounts in rape-seed and fish oil, with erucic acid being less abundant. Myristoleic acid (14:1n–7), another minor dietary monounsaturate, is associated primarily with dairy fat.

Cohen and Wynder (3) hypothesized that the switch from a low-fat diet containing a high proportion of monounsaturates to a diet high in saturated fat may have contributed to the rise in...
cancer incidences, including that of breast cancer, in modern industrial societies. Consumption patterns including a high intake of oleic acid derived from olive oil are more typical of Mediterranean than of northern European or American populations. Geographic variations in breast cancer incidence parallel these consumption patterns (4). Recent case-control studies done in Mediterranean populations have yielded evidence of a protective association between oleic acid or olive oil consumption and breast cancer (5–9). An adverse association reported in an earlier study (10) appears to have arisen through confounding by socioeconomic status (11). Studies based on populations outside of the Mediterranean region generally yield evidence of no protective association with monounsaturated fat consumption (12, 13) or even a deleterious association (14, 15), although a few studies have found some evidence of a protective association at the highest intakes (16, 17).

Most studies have used dietary questionnaire–based methods. Few studies have used a long-term biomarker reflecting fat stores (adipose tissue). Among biomarker-based studies, none observed a significant association between monounsaturated fatty acids and breast cancer (18–22); however, none of these studies included a Mediterranean population. Studies based on populations with a wider range of fatty acid intakes would be informative. We conducted a case-control analysis using the monounsaturated fat content of adipose tissue obtained in the EURAMIC (European Community Multicenter Study on Antioxidants, Myocardial Infarction, and Breast Cancer) Study, which includes populations from both northern and southern Europe, to examine whether oleic acid or monounsaturates as a whole are indeed associated with breast cancer. The primary hypothesis under exploration is that increased stores of oleic acid, the major monounsaturated, are inversely related to breast cancer in postmenopausal women. The association of other monounsaturates with breast cancer in these women was also explored.

SUBJECTS AND METHODS

Subjects and study design

The EURAMIC Study’s basic design and specific features of the study’s recruitment, response rates, and findings with respect to established risk factors were published previously (23, 24). To summarize briefly, the EURAMIC Study design involved the use of adipose tissue antioxidant concentrations to evaluate the potential role of antioxidants in breast cancer and myocardial infarction. Newly diagnosed cases of primary breast cancer (International Classification of Disease [ICD]-O 174) occurring among postmenopausal women aged 50–74 y with histologically confirmed ductal carcinomas, tumors <5 cm, axillary lymph node staging less than N3, and no distant metastases at the time of discharge were recruited between 1990 and 1992. Five centers participated: cases were drawn from surgical and gynecologic units of local hospitals in Berlin; Coleraine, Northern Ireland; Malaga, Spain; Zeist, Netherlands; and Zurich, Switzerland. Control subjects were drawn at random from women with no history of breast cancer. Control selection methodologies were designed to maximize internal validity within each recruitment center. Centers anticipating low response rates from use of population registries (Coleraine, Malaga, and Zeist) based selection on patient lists of the cases’ general practitioners. Berlin and Zurich drew control subjects from population registries.

The measured monounsaturated fatty acids included myristoleic, palmitoleic, cis-vaccenic, oleic, eicosenoic, and erucic acids. A standardized algorithm designed to identify unreliable assays through discordance between actual sample weight and total fat weight estimated chromatographically by using an internal standard was applied to these data (23). Assays flagged as invalid were excluded. CVs were determined from quality-control samples included in the analysis runs. The overall CV was 16% for myristoleic acid, 6% for palmitoleic acid, 2% for both cis-vaccenic and oleic acids, 7% for eicosenoic acid, and 9% for erucic acid (in most assays erucic acid was below the limit of detection).

After simple descriptive statistics were stratified by disease status, logistic regression models were used to provide an estimate of effect and to control for potential confounders. In addition to the fatty acids, measured risk factors included age, body mass index, oral contraceptive use, use of exogenous hormones, history of breast cancer in mother or sister, parity, socioeconomic status, current and past smoking habits, current alcohol...
drinking, and age at birth of first child, menarche, and menopause. All risk factors showing a significant correlation with any of the individual monounsaturated fatty acids within any center were included in the adjusted models. These risk factors included age, body mass index, parity, age at birth of first child (modeled as separate variables for ages < 25 y, 25–34 y, and > 34 y), and family history of breast cancer (presence of breast cancer in mother or sister). All analyses were conducted by using SAS statistical analysis software (version 6.11; SAS Institute Inc, Cary, NC). Significance was set at \( P < 0.05 \). Unconditional logistic models were used for most analyses, whereas logistic regression models conditioned according to recruitment center and 5- y age interval were used for analyses, with the entire study population pooled to maintain the matching used in recruitment.

RESULTS

Of the 721 women meeting the study’s inclusion criteria, valid adipose tissue fatty acid data were obtained from 642 and were included in the present analyses as delimited by center (Table 1). The relations between established breast cancer risk factors in the EURAMIC Study and details regarding subject response rates were published previously (24). To summarize, higher body mass index, greater age at birth of first child, and family history of breast cancer showed strong and significant relations to breast cancer. Smoking, drinking, and a history of benign breast disease also showed modest associations with breast cancer, although not significant ones.

The 14-, 20-, and 22-carbon monounsaturates are minor constituents of adipose fat, averaging < 1% of the total fatty acids in control subjects (Figure 1). cis-Vaccenic acid is more abundant, averaging \( \approx 2\% \). Palmitoleic is next in abundance, averaging > 6% in most centers, but oleic acid is by far the most common monounsaturated fat in adipose tissue, averaging > 40%.

A simple comparison of mean fatty acid percentages in cases and control subjects for each of the study centers showed sharply lower mean oleic acid concentrations among cases in Malaga. Outside of Malaga, cases and control subjects had similar oleic acid concentrations. cis-Vaccenic acid was modestly higher among cases in 4 of 5 centers, whereas palmitoleic acid was lower in 3 of 5 centers. Of the minor monounsaturates, the 14-carbon isomer showed a tendency toward lower concentrations in cases and the 20- and 22-carbon isomers showed little consistent difference between cases and control subjects. Erucic acid was, however, far more concentrated in the Berlin population than in the others, and within that population it was more common among cases.

To assess the statistical strength of the associations between the monounsaturates and breast cancer and to control for the potential effects of other risk factors, unconditional logistic regression analyses were carried out for each center (Table 1). Oleic acid had a significant protective association with breast cancer in Malaga [odds ratio (OR): 0.40; 95% CI: 0.28, 0.58]. In contrast, most of the other centers yielded ORs > 1, although only the OR for Zeist was significant after adjustment for other risk factors (OR: 2.36; 95% CI: 1.01, 5.50). Palmitoleic acid yielded ORs < 1.0 in 3 of 5 centers, being significant in Coleraine (OR: 0.50; 95% CI: 0.28, 0.88) and Berlin (OR: 0.16; 95% CI: 0.03, 0.78). Adjusted ORs for cis-vaccenic acid were > 1.0 in 4 of 5 centers, being significant only in Malaga (OR: 4.43; 95% CI: 1.68, 11.68). None of the center-specific ORs for the other monounsaturates were significant except for myristoleic acid in Berlin (OR: 0.20; 95% CI: 0.04, 0.91). Erucic acid was below the limit of detection in most samples, and < 0.01% for most samples in which it was detected. Berlin was the only center with a substantial number of detectable non-zero erucic acid values. Modeling it as a three-level ordinal variable (below detection and below or above the median among samples with detectable erucic acid concentrations) yielded a protective but not significant OR (0.58; 95% CI: 0.30, 1.11).

Regression models of the combined population from all centers provided a summary of associations for the entire study population (Table 2). Models were conditioned by center and age, with the inclusion of other risk factors as covariates. Palmitoleic and oleic acids were both inversely associated with breast cancer when all centers were combined. Associations for the other monounsaturates were weaker.

Whereas oleic acid appeared inversely correlated with breast cancer in the pooled population, the center-specific results showed that this relation was largely derived from the strong relation within Spain. In control subjects, mean adipose tissue concentrations of oleic acid were significantly higher in the

### TABLE 1

Odds ratios from unconditional logistic regression models for individual monounsaturated fatty acids by center

<table>
<thead>
<tr>
<th>Fatty acid variable</th>
<th>Coleraine ( (n = 193) )</th>
<th>Zeist ( (n = 121) )</th>
<th>Berlin ( (n = 62) )</th>
<th>Zurich ( (n = 126) )</th>
<th>Malaga ( (n = 124) )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Myristoleic (14:1)</td>
<td>( 0.74 ) (0.45, 1.22)</td>
<td>( 0.99 ) (0.60, 1.63)</td>
<td>( 0.20 ) (0.04, 0.91)</td>
<td>( 0.64 ) (0.31, 1.31)</td>
<td>( 2.02 ) (0.46, 8.83)</td>
</tr>
<tr>
<td>Palmitoleic (16:1)</td>
<td>( 0.50 ) (0.28, 0.88)</td>
<td>( 1.54 ) (0.79, 2.98)</td>
<td>( 0.16 ) (0.03, 0.78)</td>
<td>( 0.52 ) (0.26, 1.03)</td>
<td>( 1.13 ) (0.36, 3.55)</td>
</tr>
<tr>
<td>cis-Vaccenic (18:1n−7)</td>
<td>( 0.84 ) (0.56, 1.26)</td>
<td>( 1.47 ) (0.92, 2.34)</td>
<td>( 1.02 ) (0.47, 2.21)</td>
<td>( 1.31 ) (0.84, 2.03)</td>
<td>( 4.43 ) (1.68, 11.68)</td>
</tr>
<tr>
<td>Oleic (18:1n−9)</td>
<td>( 1.23 ) (0.66, 2.27)</td>
<td>( 2.36 ) (1.01, 5.50)</td>
<td>( 0.38 ) (0.07, 2.08)</td>
<td>( 0.83 ) (0.42, 1.64)</td>
<td>( 0.40 ) (0.28, 0.58)</td>
</tr>
<tr>
<td>Eicosenoic (20:1)</td>
<td>( 1.59 ) (0.94, 2.68)</td>
<td>( 0.80 ) (0.45, 1.40)</td>
<td>( 1.08 ) (0.47, 2.53)</td>
<td>( 2.22 ) (0.86, 5.73)</td>
<td>( 0.60 ) (0.32, 1.13)</td>
</tr>
</tbody>
</table>

\(^1\)95% CIs in parentheses. \( n \) = number of subjects contributing adipose tissue fatty acid data. For Zeist, \( n \) is 1 less for cis-vaccenic because of a missing value for 1 subject. Odds ratios are based on the difference between the 75th and 25th percentiles from the control population (pooled dataset): myristoleic = 0.33; palmitoleic = 3.22; cis-vaccenic = 0.49; oleic = 4.86; and eicosenoic = 0.17. The covariates were age, body mass index, age at birth of first child, and family history of breast cancer.

\(^2\)Age at birth of first child (25–34 y and > 35 y) were combined into a single variable for this center to provide adequate stratum-specific numbers.
Spanish population (55%) than in the German population (46%), which had the next highest concentration. To determine whether a protective association manifests only at high background concentrations of oleic acid, further analyses were restricted to the upper quartile of the oleic acid distribution among the non-Spanish population. Even within this subpopulation, oleic acid showed a positive, albeit nonsignificant, association with breast cancer, in contrast with the results in Spain (data not shown).

The strong inverse association observed between oleic acid and breast cancer in Spain could conceivably have been secondary to the positive association observed between breast cancer and total polyunsaturates (Figure 1). To determine the relative importance of oleic acid compared with other individual monounsaturates, total polyunsaturates, and total saturates, a forward selection algorithm was used. Oleic acid was the most significant fatty acid term in these models. It retained a significant inverse association with breast cancer regardless of which other fatty acid was included in the model. The only other fatty acids that showed significant associations with breast cancer when oleic acid \((P = 0.001)\) was already included in the model.
TABLE 2
Odds ratios from conditional logistic regression models of breast cancer by individual monounsaturated fatty acids: all centers pooled

<table>
<thead>
<tr>
<th>Fatty acid variable</th>
<th>Without covariates</th>
<th>With covariates</th>
</tr>
</thead>
<tbody>
<tr>
<td>Myristoleic acid (%)</td>
<td>0.78 (0.59, 1.03)</td>
<td>0.77 (0.57, 1.03)</td>
</tr>
<tr>
<td>Palmitoleic acid (%)</td>
<td>0.74 (0.54, 1.01)</td>
<td>0.68 (0.49, 0.93)</td>
</tr>
<tr>
<td>cis-Vaccenic acid (%)</td>
<td>1.42 (1.11, 1.83)</td>
<td>1.29 (0.98, 1.69)</td>
</tr>
<tr>
<td>Oleic acid (%)</td>
<td>0.69 (0.55, 0.86)</td>
<td>0.64 (0.51, 0.81)</td>
</tr>
<tr>
<td>Total 18 monounsaturate (%)</td>
<td>0.68 (0.54, 0.87)</td>
<td>0.62 (0.48, 0.80)</td>
</tr>
<tr>
<td>Eicosenoic acid (%)</td>
<td>1.08 (0.82, 1.43)</td>
<td>1.11 (0.84, 1.49)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Ratios</th>
<th>Without covariates</th>
<th>With covariates</th>
</tr>
</thead>
<tbody>
<tr>
<td>18:16 cis monounsaturates</td>
<td>1.07 (0.90, 1.26)</td>
<td>1.08 (0.90, 1.29)</td>
</tr>
<tr>
<td>20:18 cis monounsaturates</td>
<td>1.08 (0.88, 1.33)</td>
<td>1.15 (0.93, 1.43)</td>
</tr>
<tr>
<td>20 + 22:18 cis monounsaturates</td>
<td>1.02 (0.85, 1.22)</td>
<td>1.08 (0.89, 1.30)</td>
</tr>
</tbody>
</table>

1 95% CIs in parentheses. Odds ratios are for the difference between the 75th and 25th percentiles in the control population. See Table 1 for actual percentiles. All models were conditioned for recruitment center and age. Results exclude a potential low outlying value of 16.1n7 and “zero” values for 18:1n7 and 20:1n9 (a total of 10 for the former and 5 for the latter). Results with these values included were similar.

2 Covariates include body mass index, nulliparity, age at birth of first child, and history of breast cancer in the immediate family.

3 Percentage of total adipose tissue fatty acids.

DISCUSSION

Our results do not show a consistent protective relation of monounsaturated fatty acids with postmenopausal breast cancer. Oleic acid showed a stronger relation with breast cancer than any other monounsaturated, driven by a powerful inverse association within the Spanish center. This finding is consistent with evidence from several recent studies in Mediterranean populations, suggesting that olive oil consumption may protect against breast cancer. Outside the Spanish center, however, oleic acid showed an inconsistent association with breast cancer in 3 centers and not in a protective direction. This finding does not necessarily contradict the olive oil hypothesis. Olive oil constitutes a primary source of oleic acid in Spain (6), whereas animal fats rich in oleic acid typically contribute much more to oleate intake in populations from the nations with the other European study centers. Endogenous synthesis from saturated fats may also contribute more to oleic acid stores when monounsaturated fat intakes are lower. Therefore, oleic acid may have been a marker of olive oil consumption in Spain, the only center at which high olive oil consumption was expected, but was not in other centers. Results from the non-Spanish centers suggest that any protective effect of olive oil or other monounsaturated fat intake seen was not due to elevated tissue stores of oleic acid per se.

Evidence of an association for other monounsaturates with breast cancer was strongest for cis-vaccenic and palmitoleic acids. The association for cis-vaccenic acid was in the same direction for 4 of 5 centers yet was not significant when the results for all centers were combined. The statistically strong but directionally opposite associations of oleic and cis-vaccenic acids with breast cancer in Malaga raise the possibility that confounding may have been involved in the associations between those fatty acids and breast cancer. Effect estimates for cis-vaccenic acid showed no consistent variation with oleic acid concentrations, however, and the estimates for oleic acid were stable when analyses were stratified by tertile of vaccenic acid (results not shown). The weak statistical strength of the cis-vaccenic results cautions against giving them much weight.

Palmitoleic and myristoleic acids showed associations in a protective direction for the same 3 centers. In the other centers, palmitoleic acid appeared deleterious whereas myristoleic appeared neutral in Zeist; this pattern was reversed in Malaga. The fact that palmitoleic acid is found in fish oils raises the possibility that these findings reflect the protective effects of fish consumption. However, the poor correlation between the major n-3 component of fish oil, docosahexaenoic acid, and palmitoleic acid in those centers where an inverse association was observed (Pearson’s r = −0.27, 0.11, and −0.12 for Berlin, Zeist, and Coleraine, respectively) makes that unlikely.

Another possible interpretation is that higher concentrations of palmitoleic acid reflect a reduced need for synthesis of other medium-chain fatty acids. When dietary sources are in short supply, including situations of essential fatty acid deficiency, endogenous synthesis is increased, which could reduce palmitoleic acid stores. Although the ratios of 18-carbon to shorter or longer monounsaturates were in fact associated with breast cancer (Table 2), monounsaturates may also be synthesized from saturated fats through desaturation. Analyses adding a term for total saturated fat as well as the ratio terms to the models are not shown, but yielded similar patterns of association that were not significant.

To explore the potential effect of the disease process on fatty acid concentrations, the correlation between each fatty acid and size of tumor at diagnosis was examined. No significant correlation was observed for any of the studied fatty acids and tumor size. The number of days between surgery and biopsy also varied, including situations of essential fatty acid deficiency, endogenous synthesis is increased, which could reduce palmitoleic acid stores. Although the ratios of 18-carbon to shorter or longer monounsaturates were in fact associated with breast cancer (Table 2), monounsaturates may also be synthesized from saturated fats through desaturation. Analyses adding a term for total saturated fat as well as the ratio terms to the models are not shown, but yielded similar patterns of association that were not significant.

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benign breast disease were carried out in London, Jerusalem, New York, Kuopio (Finland), and Boston. The only monounsaturated measured in all 5 studies was oleic acid. Eid and Berry (18), Caleffi et al (19), Petrek et al (21), and Zhu et al (22) found virtually no difference in mammary adipose tissue concentrations of oleic acid between cases and control subjects, whereas London et al (20) found no difference in median gluteal adipose tissue. Petrek et al (21) and London (20) did find elevated risk estimates for the highest concentration of oleic acid in adipose tissue, although in neither instance were the risk estimates significant. In Petrek et al’s study the OR was 1.47 (95% CI: 0.71–3.03) for the upper compared with the lowest quartile and in London’s study the OR was 1.2 (95% CI: 0.7–1.9) for the upper compared with the lowest quintile. Although these studies differed in design, particularly in the way control subjects were selected, their results are compatible with our findings of a generally weak, positive association between oleic acid concentrations and breast cancer outside of the Mediterranean center.

The other monounsaturates showed little association with breast cancer in the other studies (18, 20–22). The narrow range of exposures expected for studies in women with a relatively homogeneous diet from a single catchment area could make an underlying association more difficult to detect. The use of mammary tissue as the source of samples in most of the previous studies could have led to disease-related changes in local fat composition that masked underlying exposure-disease relations, although there was no indication of this. In addition, only 2 of the studies controlled for other established risk factors, which could have confounded their results. Alternatively, the relation observed for palmitoleic and cis-vaccenic acids in the current study could have arisen by chance. Although the association for palmitoleic acid met the $P < 0.05$ criterion for significance with a two-tailed test in the pooled population, a correction for multiple comparisons would have pushed the results above this threshold.

The potential for selection bias secondary to the low control response rates was a possible source of the observed results. This is an unlikely explanation for the strong protective relation with oleic acid in Malaga because that center had the highest response rates for both control subjects and cases (each > 96%). Nor did the center with the lowest control response rates (Zurich) display results consistently different from the other northern European centers for any fatty acid.

The potential for confounding by established risk factors was addressed through multiple logistic regression. All reported risk estimates are based on models including age, body mass index, reproductive history, and family history of breast cancer. Additional models that included socioeconomic status, smoking habits, alcohol consumption, age at menarche, and age at menopause as well as the covariates enumerated previously yielded virtually identical results. Neither tumor size nor the amount of time elapsed between diagnosis and the time of tissue biopsy correlated with adipose fatty acid concentrations, which indicates no confounding by effects of the disease process on fatty acid concentrations.

One key feature of studies based on adipose tissue biomarkers is their ability to directly measure individual monounsaturated fatty acids as well as the sum of total monounsaturates, which is not possible with traditional dietary assessments. Another feature of biomarker-based studies of monounsaturated fats is the potential contribution of endogenous synthesis as well as dietary intake (29). Correlations between diet and tissue concentrations are generally not as strong for monounsaturated fatty acid classes as for the essential fatty acids (polynsaturates of the $n-3$ and $n-6$ families). The monounsaturated oleic acid is the major fatty acid component of adipose tissue. Although a recent study of Bostonians found a poor correlation between adipose monounsaturate content and estimated dietary intake ($r = 0.13$) (20), better correlation was observed in another Boston population after adjustment for energy intake ($r = 0.36$) (30) and striking differences in adipose oleate were observed in comparisons of nationalities with different fat consumption patterns (31, 32).

Nevertheless, because monounsaturated fatty acids can be synthesized endogenously as well as acquired through the diet directly, a definitive distinction between intake and internal synthesis as the source of observed tissue concentrations is not possible.

A potential advantage of adipose tissue as an index of exposure is that tissue concentrations of fatty acids may be more relevant to disease than are dietary intakes. Interindividual differences in absorption or metabolism can complicate estimates of internal dose based on reported dietary intake (33), whereas adipose tissue concentrations may better reflect the effective dose to fatty tissues such as the breast. The fatty acid profile of breast adipose tissue is reportedly representative of gluteal body fat composition, with intradividual comparisons of linoleic acid for the 2 sites yielding a correlation coefficient of 0.98 (the actual correlation coefficients for monounsaturates were not directly reported) (18). In Petrek et al’s study (21), individuals showed a significant tendency toward lower total monounsaturates and higher saturates in their breast than in their abdominal adipose tissue, yet similar relations between these fatty acids and disease status were reported for measures from either site.

Several mechanisms have been proposed for a protective effect of olive oil against breast cancer. The presence of oleic acid in membrane phospholipids retards lipid peroxidation, which depends on the presence of multiple unsaturated bonds for propagation (34). An olive oil–rich diet should therefore reduce susceptibility of tissue structures to damage by free radicals. Such protection is seen in rodents fed olive rather than soy or corn oil (35). Olive oil also contains tocopherols, carotenoids, polyphenols, and other natural chemoprotectants (36, 37). These components could confer additional protection against oxidative damage, enhancing repair processes as well as augmenting resistance to peroxidation.

If incorporation of monounsaturated fatty acids protects against lipid peroxidation, why then would not all monounsaturates appear protective? Monounsaturates derived from animal sources could be associated with red meat consumption or other dietary or lifestyle factors that might enhance risk. The minor monounsaturates are also typically small components of fats or oils containing predominantly polyunsaturated or saturated fats, so the effects of these monounsaturates may be dwarfed by those of the other fatty acids acquired along with them.

The finding of a protective effect of oleic acid in Malaga is consistent with evidence obtained in the laboratory. Animal experiments indicate that oleic acid may only be protective when ingested in a vehicle both very high in oleic acid and very low in linoleic acid, as are many olive oils. Consumption of olive oil, for example, can reduce mammary tumor incidence even in comparison with safflower oil containing similar amounts of oleic acid but higher amounts of linoleic acid (38, 39). Olive oil...
provides a major portion of the dietary oleic acid intake in a typical Spanish population (6) but most oleic acid comes from other sources in northern Europe. In addition, the antioxidants supplied by olive oil may not be provided by other oleate sources (eg, animal fats).

A strong inverse association between tissue oleic acid concentrations, as well as total monounsaturated fat concentrations, and breast cancer occurred in the Spanish study population. These findings are biologically plausible and consistent with results from dietary studies supporting protective effects of an olive oil–rich diet against breast cancer. No consistent protective association with oleic acid stores was observed in the study’s non-Spanish population, however. These results suggest that increased tissue stores of oleic acid in and of themselves are unlikely to confer significant protection against breast cancer in populations consuming a typical Western diet. The strong inverse relation between oleic acid stores and breast cancer in the Spanish population may have been due to olive oil intake, to a protective effect of other components of a traditional Mediterranean diet associated with that intake, or to some other correlate of adipose tissue oleic acid composition rather than to a direct effect of oleic acid.

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