Re: Biologic Characteristics of Interval and Screen-Detected Breast Cancers

In their recent work, Gilliland et al. (1) have shown that interval breast cancers, defined as cancers detected within 12 months after a negative mammography, are frequently high-grade, rapidly growing, and aggressive cancers. In particular, tumor proliferation rate and p53 overexpression are independent determinants of interval breast cancers, and these characteristics are seen more often among patients who are younger than 50 years of age. These features are reminiscent of what is observed for breast cancers associated with mutations in the BRCA1 gene (BRCA1-BCs) (2–4). The high proliferation rate of hereditary breast cancers and the resulting risk of interval cancer raise the important question of medical management of individuals at high genetic risk of breast cancer. In this respect, international published guidelines have recommended that mammographic screening should be carried out annually (5,6). However, based on the results of Gilliland et al. (1), it can be anticipated that even a period of 1 year, instead of the 2 years usually used in mass screening programs, might not fit with the biologic characteristics of BRCA1-BCs, which are close to those of interval breast cancers.

Although decreasing the interval between mammograms may theoretically reduce the risk of interval cancers, this option has been poorly investigated. To explore the lowest acceptable interval between mammograms that would be acceptable to patients, we studied all women who attended a cancer genetic clinic during a 1-year period. Specifically, to these women, we presented an explanatory letter and a questionnaire to be filled in before their consultations. Patients were asked to indicate their preference among five mutually exclusive intervals: every 3 months, every 6 months, every year, every 2 years, and I don’t know.

Among the 145 eligible women, 138 filled in the questionnaire (Table 1). Almost 40% (n = 55) of the subjects had a history of cancer; the mean age of patients was 44.5 years (standard deviation = 13.3 years). A majority of patients, 57.2% (n = 79) indicated a preference for an annual examination; only 28.3% (n = 39) indicated a preference for an interval of 6 months or less (Table 1).

An important element that emerged from our study is the low proportion of patients who would accept a shorter interval between mammograms than that recommended in international guidelines on hereditary breast cancer risk.

Table 1. Patients’ responses about acceptability of various intervals between mammograms among women attending a cancer genetic clinic over a 1-year period

<table>
<thead>
<tr>
<th>Interval</th>
<th>No.</th>
<th>Percentage</th>
<th>Cumulative</th>
</tr>
</thead>
<tbody>
<tr>
<td>Every 3 months</td>
<td>1</td>
<td>0.7</td>
<td>0.7</td>
</tr>
<tr>
<td>6 months</td>
<td>38</td>
<td>27.6</td>
<td>28.3</td>
</tr>
<tr>
<td>1 year</td>
<td>79</td>
<td>57.2</td>
<td>85.5</td>
</tr>
<tr>
<td>2 years</td>
<td>19</td>
<td>13.8</td>
<td>99.3</td>
</tr>
<tr>
<td>I don’t know</td>
<td>1</td>
<td>0.7</td>
<td>100</td>
</tr>
<tr>
<td>Total</td>
<td>138</td>
<td>100</td>
<td></td>
</tr>
</tbody>
</table>
management (5,6). If 6 months is a relevant interval to screen hereditary breast cancer, to reduce the risk of interval breast cancer, only a few women will favor this strategy.

Because there is a low, if any, screening cost for the high-risk women themselves in France, we assume that economic reasons do not explain the preference for a longer screening interval. Conversely, the psychologic impact or medical factors, such as the theoretical risk of radiation associated with mammography, could affect the patients’ opinions.

Management of high-risk women appears, once more, to present a potential conflict between efficacy and patient preference. If the strategy of screening more frequently than once yearly is proven to reduce mortality, the reluctance of women to accept such a screening program may represent a barrier to its implementation. The same phenomenon is observed for prophylactic mastectomy for which a woman’s acceptance of the intervention increases with the age at which it is performed, whereas the efficacy of surgery decreases (7).

Finally, since interval cancer and BRCA1-BC phenotypes overlap largely, it could be important to screen for BRCA1 germine mutation in patients with cancers that have characteristics suggestive of BRCA1 mutations, including interval tumors missed by annual screening. Encouraging results were obtained when we searched for BRCA1 mutations in women with tumors selected only by individual morphoclinical parameters. This search identified BRCA1 gene carriers who would have been overlooked if pedigree information was the sole factor taken into consideration. Consequently, it would be possible to offer to these patients, as well as their apparently unaffected relatives, appropriate medical interventions for their high risk of bilateral breast and ovarian cancers.

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REFERENCES

NOTES
Supported by the Paoli-Calmettes Institute, INSERM, and grants from Association pour la Recherche sur le Cancer and la Ligue Nationale Contre le Cancer.

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Editor’s note: Frank D. Gilliland et al. declined to respond to the correspondence by François Eisinger et al.