Concerns About Recommending Routine Screening Mammograms for Women Aged 40-49 Years

The controversy concerning the usefulness of screening mammography in women younger than 50 years continues. In general, consistently overlooked are two factors that should bear heavily on screening recommendations, particularly as they pertain to national policy: 1) understanding why screening is more beneficial after as opposed to before age 50 and 2) assessing the societal cost of routine screening in younger women.

Pivotal to this discussion—and unavailable from any of the studies—is the menopausal status of the patients being screened. Biologic age is more important than chronologic age. Without ovarian estrogen production, menopause occurs, the glandular tissue of the breast involutes, and cancerous nodules become more apparent. Therefore, screening is going to be as advantageous to a woman who is postmenopausal at age 48 as it is to a woman at age 55 or older. The reported screening studies have been conveniently designed on the basis of the subject’s date of birth (age) rather than on the basis of the appropriate standard, i.e., the menopausal status of the subject. In no study were mammograms stopped in the group younger than 50 when they reached their 50th birthday. For example, everyone continued to have mammograms into their 50s in all but one of the five Swedish study groups. In the remaining study group, at least half of the subjects did so (1). Therefore, not only was the menopausal status ignored, but also any beneficial effect of screening before 50 could not be distinguished from that of screening after 50.

However, now that screening mammograms have been recommended for women younger than 50, the societal cost of routine screening in women 40-49 years old should be considered. The average cost of a screening mammogram in the United States is $125. The U.S. Bureau of the Census states that there are currently 20,050,000 women in the United States in the age range of 40-49 years. Simple arithmetic reveals that, if every woman in this age group in the United States obtained a screening mammogram this year, the total cost would be $2.5 billion. To put this into perspective, the entire 1997 budget for the National Cancer Institute (NCI) is $2.15 billion. Of this amount, only one seventh ($300 million) is allocated for breast cancer research. At this rate, less money is allocated by the NCI to research all cancers than it would cost for all women aged 40-49 years to receive a screening mammogram this year. This does not include the amount spent on further diagnostic tests necessary to rule out cancer in the 10% of mammograms of breasts falsely considered to harbor cancer. The inescapable conclusion is that recommending screening in women 40-49 years old is a relatively costly step that is based on controversial data. Hence, a cost–benefit analysis seems in order—$2.15 billion for screening versus $300 million for research.

In our opinion, the answer lies beyond screening mammograms, particularly in younger women. If the war against breast cancer is to be won, the focus of funding in this country must go beyond spending society’s money on mammograms but instead should be on providing better funding to explore new means of diagnosis, treatment, and prevention.

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Baseline Apoptosis of Tumor Cells as a Response Predictor to Chemotherapy

Milross et al. (1) recently reported that the antitumor effect of paclitaxel is correlated with paclitaxel-induced apoptosis and baseline apoptosis in a mouse experimental model. In that report, the authors concluded, “Both the extent of pretreatment apoptosis and the paclitaxel-induced percentage of apoptosis may be useful predictors of response to the drug.” Apoptosis is an important mechanism of cell death involved in the antitumor effect of chemotherapeutic DNA-damaging drugs (2,3). The apoptotic pathways leading to apoptosis in tumor cells depend on the chemotherapeutic substance used. Apoptosis induced by most chemotherapeutic drugs is mediated by the tumor suppressor protein p53 (4), whereas other drugs, such as paclitaxel, seem to activate, at least in part, p53-independent apoptotic pathways (5).

We recently showed that a statistically significant relationship exists among the antitumor effect of cisplatin-based chemotherapy, the overexpression of the p53 oncoprotein, and cisplatin-induced apoptosis in women with locally advanced cervical carcinoma (6). Patients responding to chemotherapy showed a higher frequency of p53-positive cells than nonresponders. In that study, a statistically significant relationship was observed between p53 immunostaining and apoptosis of autologous tumor cells both before and after chemotherapy, whereas p53 expression was not correlated with MIB1-positive proliferating cells in a previous study (7). On the basis of these premises, we investigated whether responsiveness to cisplatin-based chemotherapy in women with squamous cell carcinoma of the cervix was associated with pretreatment overexpression of p53 and increased apoptosis of autologous tumor cells.

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