only palpation, as Daggett and others have suggested (Lancet 1: 483, 1981). Because of the frequent unsatisfactoriness of medical management for long-term hypoglycemia if a tumor is missed in these patients with negative preoperative imaging, however, the potential benefits of PVS is substantial. We have convincingly demonstrated that PVS is the single best preoperative localizing study and that intraoperative ultrasound (IOUS) is the single best intraoperative localizing maneuver. From a patient's perspective, if one had a rare, potentially life-threatening disease that had limited medical options for treatment, what would one want? From the viewpoint of cost-effectiveness, would it be correct to withhold a study that provides useful localizing information in at least three of four patients? The most cost-ineffective result would be unsuccessful surgery with persistent hypoglycemia. We have successfully avoided that problem in all but one of 12 patients with the methods described. Because of the rare nature of the problem and the remarkable success of our study (92%) in this subset of insulinoma patients with negative preoperative arteriographic studies, one can only do the same or worse by eliminating either PVS or IOUS, and not better.

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March 8, 1991

Dear Editor:

The article “Mastectomy Following Preoperative Chemotherapy” by Broadwater et al., published in the February issue of Annals of Surgery, contains misleading conclusions based on inappropriate comparisons between small and widely disparate groups of surgical patients. The preoperative chemotherapy group received less extensive surgery (12% modified radical mastectomy) compared with the mastectomy-alone group (61% modified radical mastectomy). Details of postoperative chemotherapy and radiotherapy are omitted.

The authors observe that there is no statistically significant difference between groups with respect to wound infection, necrosis, or delay in institution of postoperative chemotherapy, but fail to acknowledge that the trends observed are contrary to their null hypothesis (and could, conceivably, achieve statistical significance given a larger sample size). Stratification to determine differences in complication rates between appropriate groups by controlling such parameters as tumor size, local grave signs, or extent of surgery is not done. The “statistically significant” decrease in seroma rate observed in the preoperative chemotherapy group is not surprising because only 12% of that group received a full axillary dissection (versus 61% in the mastectomy-alone group). Although there was no significant difference between groups in the number of lymph nodes in the operative specimens, the numbers of nodes obtained are quite small (and documentation of how the nodal statistics are derived is not provided).

The seroma rate of 28% in the mastectomy-alone group seems unusually high when compared with other modern surgical series.

The authors observe a significant decrease in overall survival among neoadjuvant patients when chemotherapy was delayed more than 30 days, but are unable to stratify this by stage or performance status. Similar analysis of the mastectomy-alone group is not provided. Although “significance” was not achieved between the 30% of neoadjuvant patients and the 20% of the “control” patients whose postoperative systemic therapy was delayed, there is an absolute difference that might become significant with larger sample size. If delaying postoperative chemotherapy truly imparts a negative survival advantage, preoperative chemotherapy could conceivably be detrimental to survival.

The authors summarize that patient survival has improved with the use of preoperative therapy, but such a claim has been substantiated by neither their own study nor by randomized prospective trials comparing preoperative with standard postoperative chemotherapy. The case for neoadjuvant chemotherapy has been largely based on inappropriate comparisons between outdated historical control groups who received no chemotherapy and highly selected, favorable subgroups from nonrandomized neoadjuvant trials. At the Medical College of Virginia, a group of 118 patients with stage III breast cancer (1983 AJCC criteria, including 13 patients with stage IIIB inflammatory disease) treated with primary surgery and standard postoperative chemotherapy for positive nodes demonstrated a median survival of 69 months. By comparison, the median survival of 54.3 months cited by the authors does not constitute an improvement in patient survival. Similarly modern prospective series using postoperative chemotherapy for locally advanced breast cancer document overall survival rates comparable to those touted by advocates of neoadjuvant therapy.

References

JAMES L. FRANK, M.D.
Springfield, Massachusetts

June 25, 1991

Dear Editor:

The purpose of our study was to examine the morbidity of aggressive preoperative chemotherapy in patients with advanced breast cancer to (1) determine if preoperative chemotherapy was safe, and (2) evaluate if our criteria for the timing of surgery were appropriate. This paper was not designed to analyze the efficacy of preoperative chemotherapy in the management of patients with stage III breast cancer.

There seems to be much confusion regarding the nomenclature for mastectomy. Extended simple mastectomy (ESM) is a mastectomy including a level I and level II axillary lymph node dissection. Modified radical mastectomy (MRM) is the same operation with the addition of removal of the level III lymph nodes. In this study and a previous analysis that we performed, these two operations are essentially equivalent with respect to morbidity and postoperative complication rates. All patients with advanced primary breast cancer had the same postoperative chemotherapy and radiotherapy.

We agree with Dr. Frank that the sample size in our study is small and that a beta error effect could exist. This study, however, remains the only attempt in a large patient population with preoperative chemotherapy and mastectomy to define operative
Dear Editor:

We appreciate the opportunity of replying to Dr. Spratt's letter. We agree that retrospective institutional reviews require cautious interpretation. This paper sheds light on the prognosis of, and by extension, treatment requirements for women with invasive cancer detected by screening mammography. We do not think, however, that the breast cancer problem is solved.

The false-positive rate of mammography was 83% at our institution. This is similar to other large series, as outlined in the paper and discussion session. We believe that this is a major issue in breast cancer today. The high number of negative biopsies performed in the United States strains resources, is psychologically devastating to women, and may keep women from screening. Research with techniques such as stereotaxic localized sampling is necessary to reduce the need for surgical biopsy. This issue is irrelevant to the subject of the paper, however.

Similarly, Dr. Spratt's second and last points on the role of screening are important, but of little bearing on the issues we raise in the paper. Although Eddy argues that breast cancer screening is at best minimally cost effective, there are ample controlled population-based data that screening reduces breast cancer mortality.

The last point is that screening-detected cancers are more indolent. As reviewed in our paper, we and others found metastatic nodal disease in screening-detected cancer with alarming frequency (about 20%). These women fare as poorly as women with larger tumors with involved nodes. For those without nodal metastases, this and other series, some with much longer follow-up, show that these women do exceptionally well. Indeed, they do much better than T1 N0 groups in controlled adjuvant trials. This suggests that women with screening-detected, node-negative, invasive breast cancer are a subset for whom the adjuvant therapy beneficial for node-negative women in general is not necessary.

July 19, 1991

Dear Editor:

The article by M. C. Wilhelm et al. (Nonpalpable Invasive Breast Cancer, 1991; 213:600-603) contains data for which there are alternate interpretations. First, the false-positive rate was 72%, meaning that almost three fourths of all biopsies were non-beneficial. Second, the data are not population based and it is not known how many interval surancing cancers occurred between screens. Third, the types of breast cancers detected by screening are more biologically indolent and have an anticipated longer survival as a result of the length bias sampling inherent in the screening method as well as a lead time bias. Fourth, in the absence of a population based study with controls, the statement cannot be made that the probability of dying of breast cancer has been reduced.

The fourth proposition has been reviewed by Eddy (Screening for Breast Cancer, Ann Intern Med 1989; 111:389-399). Eddy, analyzing all population-based controlled clinical trials, concluded that no more than an average of 25 woman-days of life can be anticipated from mammographic screening. For every 10,000 women screened for 10 years, there will be some 2500 false-positive diagnoses with biopsy. The cost for the general population will be about 1.3 billion dollars per annum.

The purpose of my comments is to raise caution in the interpretation of non-population-based, uncontrolled retrospective studies. They do not prove that the breast cancer problem is solved, and to imply that it is in such studies creates false expectations leading to a myriad of additional medical, medico-legal, and fiscal problems.

John S. Spratt, M.D.
Louisville, Kentucky

June 19, 1991

Dear Editor:

risk and evaluate criteria for timing of surgery. No significant increase in morbidity rate was documented by this study. We are confused by Dr. Frank's comments that seroma rates of 28% are unusually high; most studies document comparable (10% to 35%) seroma rates.2

Although we did not try to make a case for preoperative chemotherapy improving patient survival, we were interested in determining if surgical complications that delayed the reinstitution of systemic therapy might impact survival. A delay in instituting postoperative therapy in advanced primary breast cancer has previously been shown by us to impact survival, and this study only confirms and supports the previous report.3 Dr. Frank is correct in stating that preoperative chemotherapy has not been shown to improve survival when compared with postoperative chemotherapy. Certainly, he would agree that all patients with advanced primary breast cancer should have aggressive systemic therapy. In addition, preoperative chemotherapy minimizes the extent of surgery required for effective local disease control. In our series, all patients had mastectomy without the need for chest wall resection, or skin grafting. It is not appropriate for him to compare survival in his series with our group of patients, because this analysis is meaningless.

We continue to support the use of preoperative chemotherapy in patients with advanced primary breast cancer. The high response rates allow surgical resection without the need for skin grafting or chest wall resection. Our study supports the safety of preoperative chemotherapy, and our criteria for the timing of surgery after aggressive chemotherapy seem appropriate. This information remains important because several cooperative groups are now using preoperative chemotherapy in clinical trials for less advanced breast cancers.

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