Hypothesis: Performance of sentinel node biopsy (SNB) instead of full axillary lymph node dissection (ALND) by inexperienced surgeons will lead to understaging of some women with breast cancer and increased costs.

Design: A decision analysis model was used to investigate the implications of SNB vs full ALND during the learning phase (60-80 procedures). This model simulates a randomized trial of 10,000 women in each arm. Data regarding the learning curve were obtained from published series.

Main Outcome Measures: Percentage of women with inaccurate staging of their breast cancer, overall survival, quality-adjusted survival, and potential costs of SNB vs ALND.

Results: Performance of SNB instead of ALND results in inability to locate a sentinel node in 38% of attempts during the learning phase (compared with 10% in later cases) and understaging in 12% of patients during the learning phase (compared with 0% in later cases). This understaging is associated with a small decrement in survival (1%-2%) and an increased risk of axillary recurrence. Sentinel node biopsy is cost-effective only when the ability to detect sentinel nodes exceeds 80%; and the cost of SNB is less than 50% of the cost of ALND.

Conclusions: To ensure accurate staging of patients with breast cancer, all surgeons should perform full ALND while learning SNB techniques. Only after documentation of accuracy of SNB (sensitivity >90%) should full ALND be omitted for women with negative sentinel nodes.
METHODS

STATEMENT OF THE PROBLEM
AND DECISION MODEL

Using decision analysis, we investigated the potential benefits of SNB, performed by experienced and inexperienced surgeons compared with full ALND for women with clinically negative axillary lymph nodes. This model simulates a randomized trial of 10,000 women in each treatment arm, estimating mean life expectancy for patients in each arm. In the ALND arm, all patients were assumed to have undergone ALND at the time of breast tumor resection, with subsequent therapy dictated by the results of ALND. In the SNB arm, all patients underwent SNB, with ALND reserved for patients in whom identification of the sentinel node was not technically possible or for those with histologically positive sentinel nodes. Women with histologically positive axillary nodes (in both groups) receive chemotherapy, whereas those with histologically negative nodes do not receive chemotherapy.

PROBABILITIES AND DATA SOURCES

Probabilities of 10-year survival were obtained from data of the Early Breast Cancer Trialists’ Collaborative Group, and converted to life expectancy calculations using the DEALE method. On the basis of these calculations, the life expectancy for node-negative patients is 21.8 years. Node-positive women have a mean life expectancy of 13.1 years if they receive chemotherapy and 10.9 years if they do not. Since ALND may have an independent effect on survival, we added a 5% survival “bonus” to patients with positive nodes undergoing ALND. The alternative hypothesis, ie, that ALND has no independent survival benefit, was tested by sensitivity analysis. Data regarding axillary recurrence in the axillae of untreated patients (those SNB patients with false-negative results) were obtained from the National Surgical Adjuvant Breast and Bowel Project (NSABP B-04). Data regarding feasibility, sensitivity, and specificity for SNB during the learning phase were obtained from Giuliano et al and Guenther et al, and contrasted to other published series (Table) in sensitivity analyses. For our initial analysis, we averaged the data from the 2 series, using 62% as the percentage of patients in which a sentinel node could be identified, and 74% for the sensitivity (defined as the percentage of node-positive axillae that were correctly identified by SNB) of detecting occult malignancy. We assumed that all nodes defined as cancer by pathologic examination actually contained cancer (specificity, 100%). The cost of ALND was based on overnight hospitalization and compared (in sensitivity analyses) with costs for outpatient ALND. Since minimal data have been published regarding the actual cost of SNB, we assumed that the cost of SNB was half the cost of ALND, and varied this ratio in the sensitivity analysis.

Our principal outcome measure, life expectancy, accounts for differences in survival and recurrence rates affected by the chosen treatment, but does not account for ALND-associated morbidity, toxic effects of chemotherapy, or cancer recurrence. We adjusted our life expectancy estimates to include quality-of-life considerations by using a modification of a Markovian cost-effectiveness analysis of Hillner and Smith. We used quality-adjusted life expectancy as the unit measure, derived by depreciating the time spent in undesirable health states according to the perceived quality of life a patient experiences during that health state. We used published quality-of-life adjustments for various cancer states. Adjustments for possible long-term morbidity from ALND were derived from Velanovich, and local expert opinion. Models were created and analyses performed using the software DATA 3.0 (TreeAge Software Inc, Williamstown, Mass). All costs and utilities were discounted over time, using a discount rate of 3%. For our initial analysis, we assumed that the patients have palpable 3-cm tumors, and that the likelihood of positive nodes is 46%.

RESULTS

Noviario (3-cm palpable tumor), 12% of patients declared “node negative” by SNB will actually harbor metastatic disease. This incorrect staging leads to a loss in life expectancy of 4 months (1.6%) for the SNB cohort, compared with patients receiving full ALND. Results of decision analysis were for ALND: life expectancy, 18.7 years; nondiscounted quality-adjusted life-years, 13.0; discounted quality-adjusted life-years, 10.2; and for SNB: life expectancy, 18.4 years; nondiscounted quality-adjusted life-years, 12.8; discounted quality-adjusted life-years, 10.0. Quality-adjusted survival figures are similar. Compared with ALND, patients receiving SNB averaged a 1.3% decrement in quality-adjusted life expectancy. Axillary recurrence occurs in 3% of patients with “negative” SNB results, with approximately half of these recurrences occurring within the first postoperative year.

SENSITIVITY ANALYSIS

As the sensitivity of SNB approaches 100%, the loss in expected survival related to the avoidance of full ALND becomes nil. For example, the expected survival decrement drops to 1 month if 90% of axillae with metastases are correctly diagnosed by SNB. As expected, the likelihood of positive lymph nodes is also a major determinant of the outcome following SNB. Fewer than 20% of patients with nonpalpable T1 tumors will have axillary nodal metastases. Consequently, patients in this subgroup experience less benefit from full ALND—1 month of better life expectancy than SNB. The incorporation of an independent survival benefit for ALND in our model and varying the percentage of cases in which a sentinel node could not be identified had little effect on the relative life expectancies for the 2 strategies. Other important variables having minimal effects on the model’s predictions include baseline survival probabilities, patient age, and quality-of-life adjustments.

Our baseline analysis assumes that patients with histologically negative nodes did not receive chemotherapy. In reality, many patients with known risk factors (eg, premenopausal, T2 tumors, aggressive histological features, and estrogen receptor negative) are treated with chemotherapy irrespective of nodal status. If we assume that 50% of node-negative patients will receive chemotherapy, then the advantage of ALND declines significantly, with ALND patients gaining only 1 month of life expectancy over SNB patients. As the number of node-negative patients receiving...
COST ANALYSIS

Because of the significant number of sentinel nodes not identified during the learning curve phase (38%), SNB is relatively expensive. Patients with unidentified sentinel nodes receive the expenses of ALND in addition to those of SNB, which include costs for additional operating room time, additional frozen sections, and radiocolloid localization (if used). The SNB arm is more expensive than the ALND arm during the learning curve phase unless the cost of SNB can be reduced to less than 40% of the cost of ALND. This implies a "break even" SNB cost of $4000 when compared with a typical overnight hospitalization, but only $1200 when compared with outpatient surgery. As surgical experience increases, with a consequent increase in the likelihood of identifying the sentinel node, the cost of SNB decreases proportionately. For example, if 90% of sentinel nodes are identified, the "break even" costs increase to $6000 (compared with inpatient ALND) and $1800 (compared with outpatient ALND).

Our analysis has some important limitations. We cannot totally reconcile the suggestion that surgeons in the learning curve phase will identify some node-positive patients who would not have been identified without any axillary surgery. We believe that the literature does not support this approach, as series of axillary node sampling have shown higher rates of axillary recurrence, as well as suggesting diminished survival. We did not consider the possibility that SNB may identify more patients with positive nodes by using sophisticated histologic techniques for sentinel node examination, but doubt that omission of the possibility of increased detection of occult metastases will change the results of our analysis.

Many authors have described the learning curves peculiar to laparoscopic surgery, and guidelines have been proposed to ensure the safety of these procedures. In a review, Gates has outlined several key points that allow surgeons to learn new procedures while benefiting patients, including avoidance of harm, peer review, and informed consent. Obviously, prevention of harm to patients must be foremost. As Copeland observes, the learning phase for SNB is different from that of laparoscopic procedures. A technical failure of SNB will not be apparent in the short term, but may lead to grave long-term effects, as opposed to the technical failures of laparoscopy, which are apparent immediately, or in the discernible future. It is impossible to ensure the accuracy of SNB during the learning phase without comparison with the criterion standard—full ALND. Hospital peer reviewers must have this information to comfortably certify surgeons in their institutions to assure that patients are not harmed by inadequate operations. Patients must be informed of an individual surgeon's "track record" regarding SNB, as well as the potential of her being understaged by the procedure. This study strongly supports the requirement for surgeons to perform full ALND during the learning phase, until the surgeon can document acceptable identification of sentinel nodes and sensitivity for detecting metastatic disease.

<table>
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<th>Source, y</th>
<th>Total N</th>
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* The results include the authors’ “learning experience” as well as later procedures.

The present analysis evaluated the implications of performing SNB by inexperienced surgeons in lieu of a formal validation period. Using decision analysis, we observed that 12% of patients declared node negative by SNB would be understaged by surgeons operating within the learning curve phase. This understaging leads to an increased risk of axillary recurrence and a decreased overall survival. The effect on a large cohort of women results in a small decrease in average life expectancy and quality-adjusted life expectancy. The high rate of unidentified sentinel nodes and the necessity for full ALND whenever the sentinel node cannot be identified increase the costs during the learning phase.
REFERENCES


