AMERICAN HEALTH CONSULTANTS

CLINICAL ONCOLOGY ALERT

Providing Evidence-based Clinical Information for 17 Years

A monthly update of developments in cancer treatment and research

American Health Consultants Home Page—http://www.ahcpub.com

CME for Physicians—http://www.cmeweb.com

The Effect of Radiotherapy Dose on Positive Pathologic Margins After Breast Conservation Surgery

ABSTRACT & COMMENTARY

Synopsis: Pathologic margin status is arguably the most important factor in patient selection for breast conservation. Terms used to describe margin status vary, and tend to be left to the discretion of the treating physician. Although most people can agree on what a negative margin is, there are no set definitions for close or involved margins. It is the latter, compromised, margins that present a challenge for the treating radiation oncologist who wishes to achieve durable local control. This study at Thomas Jefferson University Hospital could not show a dose-response effect in their group of patients with a positive surgical margin treated to high doses.

Source: DiBiase SJ, et al. *Int J Radiat Oncol Biol Phys.* 2002;53:680-686.

Dibiase and colleagues performed a retrospective analysis of stage I and II breast cancer patients treated with breast conservation surgery and radiotherapy from 1978-1994 in order to determine whether higher doses of RT are effective in lowering the risk of ipsilateral breast tumor recurrence (IBTR) in patients with positive margins. Among 733 patients treated, 641 had margin status data available. There was no attempt to achieve clear margins at the time of initial biopsy. Following a later re-excision and axillary dissection, the resection cavity bed was shaved "as if peeling an onion from the inside out." Surgical margins were declared positive if any tumor was found in the shaved margin biopsy. Twenty percent of patients (n = 132) were deemed to have positive margins by this method.

All patients received 45 Gy to the ipsilateral breast with 6MV photons via an opposed tangential field technique prescribed to the 90% isodose envelop. This was followed by either an electron boost or an iridium-192 brachytherapy boost. Patients in the low-dose group (n = 592; 92%) received 60-65 Gy while those in the high-dose group (n = 49; 8%) received 65-76 Gy. There were 213 patients who were boosted with electrons, and 428 who underwent a brachytherapy boost. Median boost dose was 20 Gy. Among the

Volume 17 • Number 8 • August 2002 • Pages 57-64

INSIDE

positive margin patients, 105 were in the low-dose group and 27 were in the high-dose group. Fifty-eight percent of the positive margin patients were boosted with Ir-192, and the rest received an electron boost. One quarter of all patients in the study received adjuvant chemotherapy, with no difference between the positive and negative margin groups. Seventeen percent of all patients received tamoxifen, but no *P* values were provided.

Median follow-up was 52 months (r, 2-154 mos). Local recurrence was scored as a tumor of the same histology and quadrant as the index lesion. The actuarial 5 and 10-year local control rates for all patients with negative margins were 94% and 88%, compared with 85% and 67% for patients with positive margins (*P* = .001). Disease-free and overall survival rates were also statistically significantly better in the negative margin group. As one might anticipate, there was no difference in the local recurrence rate between patients with negative margins who received high vs. low doses of RT (*P* = .34). In the positive margin group, 15/105 patients (14%) in the low-dose group had a local recurrence, while 3/27 in the high-dose group (11%) developed local recurrences (*P* = .67). Of the 3 high-dose recurrences, 1 patient in the 65-66 Gy range recurred, and 2 recurred after doses of 70-71 Gy. Eleven patients received 66-67 Gy, 14 received 70-71 Gy, and 1 got 76 Gy.

Multivariate analysis showed that stage and margin status were significant factors in determining local control. DiBiase et al concluded that doses beyond 65 Gy are ineffective at overcoming the adverse influence of positive surgical margins. They recommend that patients with positive margins undergo re-excision to obtain clear margins before adjuvant radiotherapy is administered.

COMMENT BY EDWARD J. KAPLAN, MD

While the Thomas Jefferson University Hospital experience engenders some factors which are peculiar to their program, it also highlights many issues that we all must consider when evaluating a patient for adjuvant radiotherapy following breast conservation surgery. The "onion peeling" resection cavity biopsy technique sounds a bit idiosyncratic, and the dichotomous positive/negative margin descriptions neglect the fine points of margin evaluation alluded to above, such as close and focally positive margins. We really don't know what the exact final margin status was for the patients declared to have positive margins. It seems likely that some number of patients actually had close margins and not focally positive margins, though after reading the paper it is probably safe to say that none had grossly involved margins. Most centers do make some effort to extirpate the whole lesion at the time of initial biopsy, rather than go back a second time as DiBiase et al almost always did. I would also suggest that patients boosted with the 2 different techniques may not achieve identical results. Low-dose rate brachytherapy boosts are not very widely practiced, and, in fact, DiBiase et al did not disclose the breakdown for the high- and low-dose groups by boost style.

Even though the numbers of patients in the study sound impressive, what this paper is really about is the 27 patients with positive margins who received high doses of adjuvant RT. A median follow-up of just more than 4 years for the entire group is on the low side based on the findings presented in similar papers, where it has been suggested that RT might delay and not prevent local recurrences. And with only 3 recurrences in this small group, it seems like it would be difficult to draw any meaningful conclusions.

Freedman et al from Fox Chase Cancer Center looked at their experience with 1262 stage I and II patients treated from 1979-1992.[1] They delivered 60 Gy

Clinical Oncology Alert, ISSN 0886-7186, is published monthly by American Health Consultants, 3525 Piedmont Rd., NE, Bldg. 6, Suite 400, Atlanta, GA 30305.

VICE PRESIDENT/GROUP PUBLISHER: Donald R. Johnston.
EDITORIAL GROUP HEAD: Glen Harris.
MARKETING PRODUCT MANAGER: Schandale Kornegay.
MANAGING EDITOR: Robin Mason.
ASSOCIATE MANAGING EDITOR: Neill Larmore
SENIOR COPY EDITOR: Robert Kimball.

GST Registration Number: R128870672.

Periodicals postage paid at Atlanta, GA.

POSTMASTER: Send address changes to *Clinical Oncology Alert*, P.O. Box 740059, Atlanta, GA 30374.

Back issues: $38.
Missing issues will be fulfilled by customer service free of charge when contacted within one month of the missing issue's date.

THOMSON
AMERICAN HEALTH CONSULTANTS

Subscriber Information

Customer Service: 1-800-688-2421

Customer Service E-Mail Address:
customerservice@ahcpub.com

Editorial E-Mail Address:
robert.kimball@ahcpub.com

World-Wide Web: http://www.ahcpub.com

Subscription Prices

United States
1 year *with* free AMA Category 1 credits: $279
(Student/Resident rate: $140).

Multiple Copies
1-9 additional copies: $206 each; 10 or more copies: $183 each.

Canada
Add GST and $30 shipping.

Elsewhere
Add $30 shipping.

Accreditation

American Health Consultants (AHC) designates this continuing medical education (CME) activity for up to 20 hours in Category 1 credit toward the AMA Physician's Recognition Award. Each physician should claim only those hours of credit that he/she actually spent in the educational activity.

AHC is accredited by the Accreditation Council for Continuing Medical Education (ACCME) to provide CME for physicians.

This CME activity was planned and produced in accordance with the ACCME Essentials.

Questions & Comments

Please call Robin Mason, Managing Editor, at (404) 262-5517 or Robert Kimball, Senior Copy Editor, at (404) 262-5413 between 8:30 a.m. and 4:30 p.m. ET, Monday-Friday.

Statement of Financial Disclosure

In order to reveal any potential bias in this publication, and in accordance with Accreditation Council for Continuing Medical Education guidelines, we disclose that Dr. Ershler is on the speaker's bureau for Wyeth and does research for Ortho Biotech. Dr. Albertini does research for Powder Ject vaccines, Inc and Lexigen Pharmaceuticals. Drs. Hawkins, Kaplan, Kotz, and Morris report no relationships related to this field of study. Drs. Canellos, Chabner, Einhorn, Goodman, Lippman, Pinedo, and Sutton did not return financial disclosures.

to patients with negative margins, 64 Gy to patients with close margins (< 2 mm), and 66 Gy to patients with positive margins. At 5 years, there was no significant difference in the incidence of IBTRs, but at 10 years patients with positive margins had a 12% cumulative LR rate and those with close margins had a 14% cumulative recurrence rate compared to 7% for patients with negative margins (P = .04). Obedian and Haffty from Yale evaluated 871 patients with a median follow-up of 13 years who were treated from 1970-1990.[2] Median dose was 64 Gy. Local control rates were 98% for patients with negative (n = 278) and close margins (< 2 mm; n = 47), and 82-83% for patients with indeterminate or positive margins. Unlike Freedman's paper, the Yale group concluded that close margins were equivalent to negative margins in local control potential. The group from the Joint Center in Boston reviewed available slides for 533 patients with early stage breast cancer treated from 1976-1987 with a median follow-up exceeding 10 years.[3] Their definition of a focally positive margin was one which contained tumor in < 3 low power fields, and close margins were < 1 mm. Doses ranged from 60-72.5 Gy. For patients with either negative or close margins, the LR rate was 7%. For patients with extensively positive margins, the LR rate was 27%. Patients with focally positive margins had an intermediate LR rate of 14%. There was no observable trend for the risk of LR among patients with margins from 0.1 to > 5 mm. Interestingly, they found that patients with focally positive margins who received adjuvant chemotherapy had a LR rate identical to those patients with negative or close margins, ie, 7%. This was not addressed in the Thomas Jefferson paper, and neither was the potential confounding factor of young age. It is well known that younger women have higher LR rates, even with clear margins.

For the time being, I feel comfortable recommending postoperative radiotherapy for patients with negative, close, and focally positive margins. Those with extensively positive margins should undergo reexcision or submit to mastectomy. Meanwhile, results from the EORTC 22881/10882 boost vs. no boost trial are pending. There were 5569 patients with early breast cancer who received 50 Gy in 20 fractions following lumpectomy. Patients with clear margins were randomized to no boost vs. 16 Gy, and those with "microscopically incomplete resections" were randomized to 10 Gy vs. 25-26 Gy. Three-year follow-up results on cosmetic outcome have been published,[4] and now we have to wait for the local recurrence data to mature. Unfortunately, the DiBiase et al study does not add much to our knowledge base, but it does serve to keep us focused on the question at hand. ■

References

1. Freedman G, et al. *Int J Radiat Oncol Biol Phys*. 1999; 15:1005-1015.
2. Obedian E, Haffty BG. *Cancer J Sci Am*. 2000;6:28-33.
3 Park CC, et al. *J Clin Oncol.* 2000;18:1668-1675.
4. Vrieling C, et al. *Radiother Oncol*. 2000;55:219-32.

Local Recurrence in Breast Cancer

ABSTRACT & COMMENTARY

Synopsis: This study performed a retrospective analysis of breast cancer patients with an isolated local recurrence. They found that prognostic factors for death included higher tumor grade, older age at diagnosis, and disease-free interval. For premenopausal patients not previously exposed to systemic therapy, the use of chemotherapy or ovarian suppression was associated with a decreased risk of death.

Source: Le M, et al. *Cancer.* 2002;94:2813-2820.

As many as 12-13% of patients will develop a local recurrence (LR) after therapy for early stage breast cancer.[1] Although factors contributing to a LR are well-described,[1] defining prognostic factors for death after an isolated LR have been limited by small studies, inability to analyze the influence of the original therapy, varying definitions of "local" and "regional" recurrence, and inadequate follow-up. Le and colleagues studied 105 women with breast cancer and an isolated LR (breast or chest wall) who were treated at a single institution. With long follow-up after the recurrence, they were able to analyze potential prognostic factors for death including the effect of original treatment choices.

The patients were identified from a database of more than 7000 patients treated from 1954-1983. At diagnosis, patients had surgically treated tumors < 2.5 cm. Treatment consisted of either mastectomy or lumpectomy with breast irradiation (45 Gy with boost to tumor bed of 15 Gy). Regardless of the type of surgery, those patients with positive axillary nodes tended to receive axillary radiation as well. Other than 7 node-positive patients treated with ovarian suppression, adjuvant tamoxifen or chemotherapy was not given.[2]

The 105 patients with an isolated LR were identified after excluding those with previous or concurrent nodal or systemic relapse. By excluding those who recurred

after January 1 1995, a long follow-up was achieved (median, 11.5 years). Fifty-seven of the 105 patients recurred again (8 isolated local, 33 distant, 16 both) of whom 52 patients died. This corresponded to 5- and 10-year overall survival rates (after the LR) of 76% and 56%, respectively, with a median survival of 12.9 years. This compares favorably with a median survival of 2.2 years when a distant recurrence was the first event.

Le et al chose to focus on the factors affecting the risk of death after a LR (this is not a study of the risks of having an LR). By univariate analysis, 3 factors were found to be significant: 1) tumor grade; 2) age at initial treatment; and 3) disease-free interval (DFI). Specifically, the risk of death was increased about 2-3 fold for grade 3 tumors, for patients older than age 60 at diagnosis, and for a DFI of less than 8 years. On the other hand, the risk of death was not influenced by the type of surgery at diagnosis, the use of radiation at diagnosis, or the original nodal status. The increased risk in older patients was felt to be due to competing causes of death.

Local treatment at the time of recurrence depended in part on the initial treatment. In the 55 patients originally treated with breast-conserving therapy, the LR was managed by mastectomy in most (82%) patients. Almost all of the 150 mastectomy patients received radiation therapy at relapse, even those previously radiated.

The benefits of systemic treatment at the time of recurrence depended on menopausal status. It appeared that both ovarian suppression and chemotherapy (CMF, FEC, or FAC) significantly decreased the risk of death in premenopausal patients, although the role of tamoxifen in these patients was unclear due to small numbers. In postmenopausal patients, there was no significant effect from tamoxifen or chemotherapy.

COMMENT BY KENNETH W. KOTZ, MD

Le et al from France report on a relatively large, single-institution retrospective study of breast cancer patients with a LR. Focusing on patients without nodal or systemic involvement, their goal was to define prognostic factors for death, and in particular to study the influence of the initial local treatment. They found that histologic tumor grade, age at initial diagnosis and DFI, but not the original stage or local treatment approach, were prognostic for death after a LR. This is consistent with other series which, in general, show that the DFI is the most reliable factor for predicting survival after a LR,[1,3] with other factors inconsistently associated with prognosis, such as initial tumor grade and stage, tumor size at recurrence, young age, and premenopausal status.[1,3] It has also been suggested that a LR after breast-conserving therapy may have a better prognosis than after mastectomy,[3-5] although this was not observed by Le et al. The 2.5 cm cut off in the study by Le et al may have reduced a bias present in many other studies where patients with larger tumors tended to get a mastectomy.[4]

In patients previously treated with lumpectomy, the standard treatment for LR usually consists of mastectomy. Five-year relapse-free survival rates are 60-75%.[3] Whether such patients could safely undergo a repeat breast-conserving approach is unknown[3], although some have noted a higher LR rate with no effect on survival.[4] A recent report does suggest that excision followed by repeat radiation therapy may be an acceptable alternative to mastectomy.[6] Le et al treated 10 patients in this manner. Five of these patients also received a second course of radiation (details not provided).

Radiation therapy is the standard local treatment for mastectomy patients, with prior gross excision recommended, even if initial systemic therapy is required for resectability.[5] The value of radiation in patients who previously received it is not well established,[3] although Le et al gave repeat radiation to 90% of such patients (treatment details and side effects not reported).

Le et al found no benefit to tamoxifen or chemotherapy in the risk of death in previously untreated postmenopausal patients after a LR. On the other hand, they found a statistically significant decrease in the risk of death after a LR in previously untreated premenopausal patients associated with the use of ovarian suppression and chemotherapy (RR, 0.2 for both). For premenopausal patients, the tamoxifen data were unreliable due to the small number of patients who received it. Because the use of systemic therapy after a LR is of unproven benefit,[3-5] its general use should be individualized. A randomized trial that addressed this issue showed that tamoxifen reduced the rate of local treatment failure and improved the 5-year disease-free survival rate from 36-59%.[7] This difference had disappeared by 8-9 years after randomization and there was no impact on the development of distant metastases or on overall survival.[3,4] Nevertheless, because of the excellent toxicity profile, hormonal therapy can be considered for patients with a LR due to the favorable toxicity profile.[3,4] The use of chemotherapy is more problematic,[3,4] even more so in previously treated patients at higher risk of drug resistance,[5] but might be reasonable in eligible patients not previously exposed to cytotoxics.[5] ■

References

1. Clemons M, et al. *Cancer Treat Rev*. 2001;27:67-82.

2. Le M. Personal Communication, July 2002.
3. Harris J, et al, eds. *Diseases of the Breast*. Philadelphia, Pa: Lippincott Williams & Wilkins, 1996.
4. Clemons M, et al. *Cancer Treat Rev*. 2001;27:83-92.
5. DeVita VT, et al, eds. *Cancer Principles & Practice of Oncology*. Philadelphia, Pa: Lippincott Williams & Wilkins, 2001.
6. Deutsch M. *Int J Rad Onc Biol Phys*. 2002;53:687-691.
7. Borner M, et al. *J Clin Oncol*. 1994;12:2071-2077.

Prognostic Significance of True Occult Axillary Metastases

ABSTRACT & COMMENTARY

Synopsis: There is, as yet, no consensus in the literature regarding the prognostic significance and subsequent clinical management of patients with axillary nodal metastases transparent to H&E staining but detectable on immunohistochemical evaluation. This study reports that results shifted over extended follow-up and concludes that there is no significant difference in prognosis between node-negative patients in comparison to those with micrometastases identified on immunostaining.

Source: de Mascarel I, et al. *Brit J Cancer*. 2002;87: 70-74.

In this report, de mascarel and colleagues reported updated results on a group of postmastectomy/axillary dissection patients with longer follow-up. They previously published findings at 10 and 15 years, and now offered data from 20 years of follow-up.

Between 1965 and 1984, 2768 women underwent modified radical mastectomy and axillary node dissection at the Institut Bergonie in France. The mean number of lymph nodes examined at the time of surgery was 14 (range, 2-29). Each node was serially sectioned using 1-1.5 mm slices perpendicular to the long axis, with a mean of 4 slices per node (range, 1-9). All slices were evaluated on hematoxylin and eosin (H&E) staining. Fifty four patients received postoperative radiotherapy, and virtually none received chemotherapy. de Mascarel et al selected a subset of 218 patients whose axillary lymph nodes were negative on H&E staining for further analysis with immunohistochemical staining, including 129 with infiltrating ductal carcinoma (IDC), and 89 with infiltrating lobular carcinoma (ILC).

Restaining with a cocktail of 5 monoclonal antibodies directed against epithelial cell antigens was performed on the original diagnostic H&E slides that were negative on routine examination. Unequivocal metastases were found by immunostaining in 13 IDC patients (10%) and 37 ILC patients (41%). All IDC metastases were located in 1 lymph node, while 26% of ILC metastases were in 1 node, 6% were in 2 and 3 nodes each, and 3% were in 4 lymph nodes. The IDC metastases were characterized as small tumor clusters in the subcapsular sinuses up to 0.2 mm, and the ILC metastases were typically irregularly distributed single cells anywhere in the entire nodal section.

de Mascarel et al's earlier results were notable for lower metastasis-free survival and overall survival for IDC patients with occult nodal metastases at 10-year follow-up. At 15-year follow-up, overall survival was not significantly different from patients without nodal metastases, but metastasis-free survival was still significantly better in the node-negative IDC group. For the ILC patients, there was never a difference in outcome for the node negative and occult node-positive groups in the previous publications. Now, at a median follow-up of 24 years for the IDC patients and 18 years for the ILC patients, neither actuarial metastasis-free nor overall survival was significantly different in comparison to the node-negative patients (P = .62 for ILC patients and P = .076 for IDC patients). There were 60/129 IDC and 19/89 ILC patients evaluable at the time of longest follow-up. Survival data were calculated from the time of surgery.

de Mascarel et al concluded that occult axillary nodal metastases detected on immunostaining do not have any prognostic significance at the time of extended follow-up for either infiltrating ductal or lobular carcinomas. They noted that their study was the only one to date that used serial macroscopic sectioning, provided extended follow-up, and differentiated between histologic types. They distinguished their technique of nodal analysis from those of other studies. Other researchers report that they most often recut blocks and find metastases with immunostains that might otherwise have been evident on H&E had more cuts been done. The French group emphasized that their findings were limited to patients with truly occult metastases. The fact that survival statistics lost their significance over time for IDC, while the statistics for ILC never showed significance, may point to a difference in the natural history of the 2 histologies. Further prospective work needs to be done to be sure that the results from this relatively small number of patients

are applicable to the universe of node negative breast cancer patients.

■ COMMENT BY EDWARD J. KAPLAN, MD

This paper makes several good points. In the discussion section, de Mascarel et al reviewed 11 other studies and showed that most of them used the standard macroscopic technique of checking one node slice on H&E transected at the major axis of the lymph node. This is despite the fact that it is widely acknowledged that this style misses many metastases. They also felt that the high percentage of "occult metastases," ie, those visible on H&E but missed because of single slice analysis, may be the reason that "all women with breast cancer" seem to benefit from adjuvant chemotherapy, regardless of lymph node status.

In my opinion, before we can know whether occult metastases have prognostic significance, we must separate out 2 distinct entities which until now seem to have been lumped together. Those entities are macroscopic metastases noted on H&E staining using a multi-slice technique, and truly occult disease identified upon restaining of the same cuts with monoclonal antibodies. It is evident that, before a judgment can be rendered, we will need large patient numbers, longer follow-up, and meticulous technique. It should be easier to handle the caseload now that many axillary dissections are performed using a sentinel node technique, which means the number of slides to be checked is reasonable. As deMascarel et al described, all of the occult metastases in the IDC group were in one node, presumably corresponding to what would be the sentinel lymph node by today's technique. It is less clear whether the same is true for ILC. de Mascarel et al never offered their selection criteria for the subset of node negative patients chosen for further study.

Dowlatshahi and colleagues, in a Medline review of papers examining micrometastases in axillary nodes, stated that the vast majority of lymph node metastases would be detected by taking 2 sections 0.3 mm apart and staining them with a single monoclonal antibody. This appears to be a practical and economically viable approach in the context of sentinel lymph node biopsies.[1] In contradistinction to the French paper, Dowlatshahi et al noted that the more recent studies have consistently shown survival differences in patients with occult metastases. However, only about half of the papers included in their review used immunostaining. Many would argue that metastases found on H&E are not really occult by definition.

Tjan-Heijnen and associates in their paper on axillary micrometastases from the Netherlands, are of the opinion that survival outcomes are dependent on the size of the nodal metastases. This speaks to the issue alluded to above. They caution that the value of adjuvant therapy can be questioned for patients with micrometastases who otherwise have favorable prognostic factors.[2]

We may ultimately find that performing multi-slice H&E staining on sentinel lymph node tissue gives us all the prognostic information we need. Perhaps immunostaining will fall out of favor after we stop using it to find "occult metastases" that were there the whole time, in slices that we never checked with H&E. This seems like the type of study that would be tedious to perform, but could be done well by a group that maintains a large repository of relatively older sentinel node paraffin block specimens, where results can be correlated with follow-up data. ■

References

1. Dowlatshahi K, et al. *Cancer.* 1997;80:1188-1197.
2. Tjan-Heijnen VC, et al. *Breast Cancer Res Treat.* 2001;70:81-88.

Resource Use for Patients Undergoing Hysterectomy with or without Lymph Node Dissection for Endometrial Cancer

ABSTRACT & COMMENTARY

Synopsis: Age and racial/ethnic differences in comorbid illness, complications, and resource use exist for patients undergoing hysterectomy for endometrial cancer. Quantification of the complexity of care is of utmost importance for allocation of sufficient resources.

Source: Brooks SE, et al. *Gynecol Oncol.* 2002;85: 242-249.

Brooks and colleagues conducted a population-based analysis of patients undergoing hysterectomy for endometrial cancer in Maryland from 1994 to 1996. Of 1281 women undergoing hysterectomy, 91% had total abdominal hysterectomy, 6% underwent vaginal hysterectomy, 2.5% underwent radical hysterectomy, and 0.3% underwent laparoscopically assisted vaginal hysterectomy. Lymph node dissection was performed in 32% of the cohort. Neither age, nor race, nor comorbid illness influenced admission to teaching hospitals. Comorbidity was documented in

56% of cases. African Americans were more likely to have one (P = .002) or > 1 comorbid illness (P = .045) than Caucasians. The most common complications were anemia (13.6%), infection/fever (12%), cardiac (9.4%), pneumonia (8%), ileus (5%), and bowel obstruction (5%). These complications occurred with higher frequency in teaching hospitals (P = .0001), in large hospitals (P = .0001), and in African American patients compared to Caucasians (P = .028). Multivariate regression analysis revealed that older age, admission to teaching or large hospitals, lymph node dissection, heart disease, and African American race were associated with significantly higher resource use. Brooks et al concluded that age and racial/ethnic differences in comorbid illness, complications, and resource use exist for patients undergoing hysterectomy for endometrial cancer. The differences in resource use for teaching hospitals may be reflective of the severity of complications, which are indirectly determined by length of stay. Given the higher costs and skills required to care for elderly women with comorbid disease and complications, quantification of the complexity of care is of utmost importance for allocation of sufficient resources for the care of women with endometrial cancer.

COMMENT BY DAVID M. GERSHENSON, MD

The study findings reported herein are important, in that they detail that advanced age and ethnicity are associated with differences in comorbid illness, complications, and resource use for women with endometrial cancer undergoing surgery in Maryland. Previous studies have documented that African American women with endometrial cancer have a significantly decreased survival rate compared with Caucasian women. This study drills down to some of the reasons for this disparity—comorbid illnesses and complication rates. Of course, this population-based study did not include those women whose comorbidity precluded surgery; such women might be treated with radiotherapy alone, hormonal therapy, or no treatment at all. As Brooks et al also point out, the African American patients in their study were more likely to be uninsured or insured by Medicaid, suggesting that survival may be linked to income level. It is not surprising that teaching hospitals had higher rates of complications and longer lengths of stay, but the precise reasons for this finding remain elusive. There apparently was no difference in the rate of comorbidity between patients admitted to teaching hospitals vs. other types of hospitals. One wonders if more advanced disease resulting in more complicated treatment played a role in this observation. This study addresses resource use in a common cancer for women and underscores the need for further study in this area. ■

Dr Gershenson is Professor and Chairman, Department of Gynecology, M.D. Anderson Cancer Center, Houston, Tex.

CME Questions

6. Which of the following regarding lumpectomy margins is true?

a. Close margins are usually considered to be < 1-2 mm by most investigators.
b. Clear or negative margins are typically those that exceed 1-2 mm.
c. Focally positive margins may show tumor that involves < 3 low power fields.
d. All of the above

7. Regarding DiBiase et al, which statement is correct?

a. More positive margin patients were treated in the low RT dose group than were treated in the high RT dose group.
b. Patients with focally positive margins did better than those with negative margins.
c. Patients with focally positive margins did worse than those with negative margins.
d. One would expect that, based on the length of follow-up in the study, most of the local recurrences that were going to happen have already happened.

8. Which of the following regarding axillary metastases is true?

a. Less than 5% of node negative patients have occult axillary metastases.
b. The percentage of patients with axillary metastases is often underestimated because of shortcuts taken in sectioning the lymph nodes.
c. Immunostaining is no better than H&E in detecting axillary micrometastases.
d. Occult axillary metastases have been shown by most investigators to have no bearing on prognosis.

9. According to deMascarel et al, which fact is cited correctly?

a. Occult lymph node metastases had a profound effect on overall survival.
b. Most occult nodal metastases were obvious on both H&E and immunostaining.
c. ILC and IDC micrometastases shared common features regarding their size and location within the lymph nodes.
d. ILC micrometastases were primarily isolated cells that could be anywhere in the lymph node.

10. Based on data from the study by Le et al, the risk of death in previously untreated patients after an isolated local recurrence is reduced in:

a. premenopausal patients by tamoxifen.
b. premenopausal patients by radiation
c. premenopausal patients by chemotherapy
d. postmenopausal patients by tamoxifen
e. postmenopausal patients by radiation

Attention Readers . . .

American Health Consultants is happy to announce that we are opening up our *Primary Care Reports* author process to our readers. A biweekly newsletter with approximately 5000 readers, each issue is a fully referenced, peer-reviewed monograph.

Monographs range from 25-35 Microsoft Word document, double-spaced pages. Each article is thoroughly peer reviewed by colleagues and physicians specializing in the topic being covered. Once the idea for an article has been approved, deadlines and other details will be arranged. Authors will be compensated upon publication.

As always, we are eager to hear from our readers about topics they would like to see covered in future issues. Readers who have ideas or proposals for future single-topic monographs can contact Managing Editor Robin Mason at (404) 262-5517 or (800) 688-2421 or by e-mail at robin.mason@ahcpub.com.

We look forward to hearing from you. ■

In Future Issues:

More on Colon Cancer