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Aggressive Surgery and Intraperitoneal Chemotherapy for Peritoneal Carcinomatosis from Colorectal Cancer

ABSTRACT & COMMENTARY

Synopsis: Peritoneal carcinomatosis from colorectal carcinoma is considered to be invariably fatal using standard surgical and chemotherapeutic approaches. Five-year disease-free survivals in approximately 25% of highly selected patients treated with aggressive surgery and intraperitoneal chemotherapy previously have been reported. This report from the Gustave Roussy Institute confirms the previous experience. Postoperative mortality was 9% and morbidity was significant, but both can be improved by patient selection. Half of the patients who relapsed did not have detectable disease in the peritoneal cavity. The role for postoperative intraperitoneal and systemic chemotherapy needs to be defined, but it seems unlikely that these results could have been obtained without first obtaining a minimal disease state through surgery.

Source: Elias D, et al. *Cancer.* 2001;9:92:71-76.

In a prospective study, patients with peritoneal carcinomatosis (PC) from gastrointestinal primaries were recently documented to have mean survival times of 6.9 months, and this condition has generally been considered to be fatal.[1] However, some highly selected patients have been reported to have prolonged (> 5 years) disease-free survivals following aggressive surgical debulking and intraperitoneal chemotherapy (IC).[1] In the current report, Elias and colleagues treated 64 patients with PC from colorectal carcinoma from January 1993 to December 1999 on 2 separate protocols. Primary sites were colonic, rectal, and aggressive histology appendiceal tumors (46, 9, and 9 patients, respectively). All patients underwent maximal surgical debulking. Patients with liver or lymph node metastases were included if the malignant disease was grossly totally resected. Patients with lung metastases or disease in the paraaortic lymph nodes were excluded. Patients were entered into the study if complete tumor resection (residual disease < 1 mm) could be accomplished. The first protocol treated 37 patients by following the surgery with immediate intraperitoneal chemotherapy (EPIC)

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consisting of mitomycin C 10 mg/m^2 on postoperative day 1 and 5-fluorouracil 500 mg/m^2 on the next 4 days. Each drug remained in the peritoneal cavity for 23 hours and was drained for 1 hour before the next day's drug was instilled. The second study of 27 patients was a phase I/II trial in which various approaches to maximize the distribution of IC and the addition of hyperthermia were explored. During this study, the doses of mitomycin C were modified and cisplatin was added in 6 patients. Data were collected prospectively and no patients were lost to follow-up. Median follow-up was 51.7 months (range, 8.1-89.3 months).

Surgery was extremely aggressive. The mean number of tumor bearing regions, resected organs, and bowel anastomoses were 7.9, 4.7, and 2.6, respectively. One fifth of the patients had colectomies and the median operating time was 444 minutes (range, 130-780 minutes). Approximately 10% of patients died during the postoperative period, 3 in each study. Four of these patients had large preoperative tumor burdens and 2 had preoperative risk factors (obesity, coagulopathy). Abdominal complications occurred in 45% of patients consisting of fistula formation, development of an abscess and/or the need for reoperation. Extra-abdominal complications occurred in approximately 55% of patients. The mean duration of hospitalization was approximately 4 weeks.

Overall and disease-free 5-year survivals for the entire group of patients were 27% and 18%, respectively. The presence of associated metastases and a large amount of peritoneal disease preoperatively were associated with significantly lower survivals (P = 0.04 and 0.019, respectively). Of the patients who developed tumor recurrence, one half remained tumor-free in the peritoneal cavity.

COMMENT BY MICHAEL J. HAWKINS, MD

The use of aggressive surgical and IC techniques for the management of patients with advanced colorectal carcinoma metastatic to the peritoneal cavity continues to be a matter of debate. This study reports a high (10%) postoperative mortality and significant (66%) morbidity associated with this approach. The postoperative complication rate can no doubt be improved with experience and patient selection and the toxicity can be justified for patients with an otherwise terminal diagnosis. However, the toxicity and cost of this approach clearly requires the conduct of clinical trials to demonstrate what, if any, roll it has to play in the management of these very ill patients. All of the patients in these 2 studies were able to undergo excellent surgical reduction of their tumor burden and it seems unlikely that such results could be obtained without initial tumor debulking. It is hard to gauge from this report the degree to which immediate IC contributed to the high complication rate given the extensive nature of the surgeries performed. In addition, half of the patients relapsed only outside of the peritoneal cavity indicating that the role of systemic chemotherapy needs to be evaluated.

Nonetheless, at the present time it is difficult to decide upon a treatment course when one has a patient who is a good surgical risk with a minimal to moderate amount of disease that is limited to the peritoneal cavity that can likely be significantly debulked (debunked—I think). Systemic chemotherapy is clearly only palliative in this situation without surgery.[2] Aggressive surgical debulking followed by either systemic chemotherapy alone or the combination of intraperitoneal chemotherapy followed by systemic chemotherapy is a logical choice for these patients and could form the basis for a randomized clinical trial. ❖

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Prognostic Factors Analysis of Melanoma Patients

ABSTRACT & COMMENTARY

Synopsis: Factors predicting melanoma-specific survival rates were analyzed in 17,600 melanoma patients with complete clinical, pathologic, and follow-up information using the Cox proportional hazards regression model. Results for patients with localized melanomas (stages I and II) demonstrated that tumor thickness and ulceration were the most important predictors of survival, and the Clark's level of invasion had a significant effect only for melanomas less than 1.0 mm in thickness. The most important predictors of survival for patients with nodal metastases (stage III) were the number of metastatic nodes, tumor burden (microscopic vs macroscopic), and ulceration of the primary melanoma. Patients with stage IV disease and nonvisceral metastases had a better survival than did stage IV patients with visceral metastases. The results of this analysis provide an evidence-based foundation for a revised staging system for cutaneous melanoma.

Source: Balch C, et al. *J Clin Oncol*. 2001;19: 3622-3634.

Accurate and universally accepted cancer staging systems are essential to accurately identify prognosis for the individual patient and to allow for comparison of treatment results among different centers. Staging systems for cutaneous melanoma stratify melanomas based upon local, regional, and distant disease and have correlated with survival.[1] Since most melanoma patients present with localized disease, the recent American Joint Committee on Cancer (AJCC) staging system for cutaneous melanoma used stage I and II to designate low- and intermediate-risk patients with localized disease.[1] Stage III identified patients with regional disease and stage IV identified patients with distant metastatic disease.[1] Several published studies have improved our understanding of prognostic factors of melanoma, and the tumor-node-metastasis (TNM) criteria and stage groupings used in the recent AJCC staging system have been shown to have many inaccuracies.[2] The prior AJCC staging system used thickness as a factor for T-stage with thresholds of 0.75, 1.5, and 4.0 mm, and the Clark's level of invasion was considered an important determinant of T-stage.[3] The variable of ulceration was not considered to be an important prognostic factor for T-stage. A primary prognostic factor for stage III disease was the dimension of the nodal involvement, while the number of nodal metastases and the distinction of microscopic vs. macroscopic nodal involvement were not recognized as clinically important.[3] Thus, a comprehensive analysis of prognostic factors of cutaneous melanoma was needed to provide a basis for a new and more accurate staging system.

This study by Balch and colleagues reports on prospectively accumulated melanoma patient data from 13 institutions and cooperative groups. The entire melanoma patient database consisted of 30,450 patients, and 17,600 of these patients (58%) had information available for the factors required for the proposed AJCC classification and stage grouping.[3] Follow-up on these patients was available for at least 5 years for 12,837 patients (73%), and 8633 patients (49%) had at least 10 years of follow-up. Six experienced clinical statisticians participated in the analysis. The prognostic variables of tumor thickness and ulceration were identified as the 2 most important independent variables in a multivariate analysis of the 13,581 patients with localized disease. The presence or absence of primary tumor ulceration was the second most powerful prognostic indicator in these patients. When the primary melanomas were divided into thickness categories (less than 1.0 mm; 1.01-2.0 mm; 2.01-4.0 mm; and more than 4.0 mm), the survival rate for ulcerated melanomas was virtually the same as for nonulcerated melanomas of the next greater category. Other significant prognostic factors included patient age (worse with increasing decades of life), site of the primary melanoma (trunk and head and neck sites worse than extremities), level of invasion (most important for the subgroup with thin melanomas less than 1.0 mm), and sex (men worse than women). Important variables for patients with lymph node metastases included the number of metastatic nodes, the tumor burden (defined as microscopic vs macroscopic) and the presence or absence of ulceration of the primary melanoma. Somewhat lower correlation with survival was also seen with the site of the primary melanoma as well as with patient's age. The number of involved nodes (1 vs 2 to 3 vs 4 or more nodes) was the most significant prognostic factor in these patients. For patients with distant metastases, the survival rates were measured in months rather than years. The most significant differences were noted with visceral vs nonvisceral (skin, subcutaneous tissue, and distant lymph nodes) sites. In addition, patients with lung metastases had a better 1-year survival than did patients with other visceral sites of metastases, but no differences were noted when 2-year survival data were compared. Balch et al

conclude that the current analysis provides an evidence-based foundation for a revised melanoma staging system.

■ COMMENT BY MARK R. ALBERTINI, MD

The melanoma prognostic factor analysis in this report is the largest ever conducted and provides a solid evidence-based foundation for a revised melanoma staging system. This revised system will be valuable for improved prognostic information for the individual patient and for better comparison of results from melanoma clinical trials. Balch et al successfully combined prospective databases to provide a large number of patients for this analysis. In addition, the length of follow-up for these patients (73% for at least 5 years; 49 % for at least 10 years; and 14% for at least 20 years) allowed for meaning comparison of survival impacts of the prognostic factors in this study. Thus, the results from this analysis represent an important contribution to our staging of melanoma patients.

The current study supports the powerful prognostic importance of ulceration of the primary melanoma. This variable of ulceration was important both for primary melanomas as well as for melanomas that had metastasized to the regional nodal basin. The biologic activity of an ulcerated melanoma has been compared to that of poorly differentiated cancers of other histologies and is considered to represent a characteristic of tumors with a greater capacity to metastasize.[3] Ulceration is clearly identified as the second most important prognostic variable behind tumor thickness in predicting survival. Balch et al also clearly identify the prognostic importance of regional nodal characteristics of number of nodes and tumor burden. Patients with stage III disease represent a heterogeneous group of patients, and accurate comparison of stage III treatment trials will require an understanding of the number of involved lymph nodes, tumor burden, and presence of ulceration of the primary tumor. In addition, ongoing investigation may identify other factors potentially relevant to prognosis and staging of melanoma patients.[4] Ongoing evidence-based analysis will be required of these new variables, and the current study provides a model for this type of analysis. ❖

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Preoperative Radiotherapy Combined with Total Mesorectal Excision for Resectable Rectal Cancer

ABSTRACT & COMMENTARY

Synopsis: Total mesorectal excision (TME) is a surgical technique using sharp dissection of the rectal fascia during resection of rectal cancer. This contrasts with traditional surgical techniques that use blunt dissection and may thus leave tissue fragments behind. The TME technique has been associated with lower local recurrence rates compared with the blunt technique. The Dutch Colorectal Cancer Group, in collaboration with the EORTC, designed a randomized trial to determine whether a short course of preoperative radiotherapy adds to the benefits of TME in early rectal cancer. Initial results at 2-year follow-up show statistically significantly better local control results for the combined modality group, and it is anticipated that an overall survival advantage will emerge with longer follow-up.

Source: Kapiteijn E, et al. *N Engl J Med*. 2001;345: 638-646.

The dutch colorectal cancer group reasoned that it is possible that rigorous surgical technique may obviate the need for preoperative radiotherapy for rectal cancer. Previously published results from the Swedish Rectal Cancer Trial and a meta-analysis by Camma indicated that there is a local control and survival benefit with preoperative radiotherapy (RT).[1,2] While the Swedish trial used a short course of radiotherapy, administered in 5 days, the Camma paper reported on various series which used 1-5 week courses. The Dutch/EORTC trial reported by Kapiteijn and colleagues is the first randomized trial to incorporate the TME technique, and a short radiotherapy schedule was coupled with it for comparison in a combined modality arm.

From January 1996 through December 1999, 1861 patients with nonfixed adenocarcinomas of the rectum were randomized to either TME alone or 25 Gy in 5 days followed by immediate TME. Patients were stratified by treating center and planned surgical procedure, ie, abdominoperineal resection (APR) or low anterior resection (LAR). There were 1805 patients eligible for evaluation, including 908 in the TME arm and 897 in the combined modality arm. Postoperative adjuvant therapy, including chemotherapy, was prohibited

except in patients who had positive surgical margins. Median patient age was 65 years, and two thirds were males. Both arms were equally balanced in terms of demographics and tumor features. The majority of patients (n = 1530, 85%) were accrued in the Netherlands, where surgeons were intensively trained to perform TME procedures using workshops, symposia, and videotapes, and world-renowned surgeon proctors were required for the first 5 cases.

Median follow-up was 24.9 months (range, 1.1-56 months). Gross total resection without tumor spillage was achieved in 1748 patients (97%), and 1653 patients (92%) were free of metastatic disease at laparotomy. No additional information on findings at the time of surgery, other than the fact that no tumor was detected at surgery in 28 patients (2%), was provided. Consistent with a previously published early report, there were no differences between the treatment arms in postoperative mortality, and negligible differences in postoperative morbidity slightly favoring the surgery alone group.[3]

Approximately two-thirds of patients in both treatment arms underwent LAR. Gross total resection rates were similar in both groups (96-97%). Median time from randomization to surgery was 14 days in the TME arm, and 21 days in the combined modality arm. Ninety-one percent of patients were treated per protocol in the combined modality arm, and 94% in the TME arm. The overall postoperative death rate was 3.4%. Two-year overall survival was essentially identical at 81.8% for the combined modality arm, and 82% for the TME arm ($P = .84$). The rate of distant metastases was also similar, at 14.8% for the combined modality arm, and 16.8% for the TME arm ($P = .87$). However, there was a statistically significant difference in local control. In the combined modality arm, the 2-year local recurrence rate was 2.4% compared with 8.2% for the TME arm ($P < .001$).

Kapiteijn et al concluded that short-term preoperative radiotherapy reduces the risk of local recurrence in patients treated with TME for rectal cancer. An effect on overall survival probably has not emerged yet because of the small number of local recurrences and the short follow-up. The benefit from RT applied to tumors at all levels in the rectum, and to all stages studied.

COMMENT BY EDWARD J. KAPLAN, MD

The Dutch trial is the first to incorporate the TME technique into a randomized trial evaluating adjuvant therapy in rectal cancer. Since a short course of 25 Gy followed by immediate surgery was the regimen used in the combined modality arm, fixed lesions could not be included. This is because downstaging of the lesions increases over weeks as reported by Francois in the Lyon R90-01 randomized trial, not over just a few days as per the Dutch trial.[4] Even very advanced lesions can be downstaged successfully in preparation for surgery.[5] Since downstaging was not a goal of the Kapiteijn study, sphincter-sparing for low-lying lesions could not be accomplished, and thus there were a lot of APRs done in both treatment arms.

It will be interesting to see whether a survival benefit does become apparent as follow-up data accrue. The local control benefit from radiotherapy, in the face of state-of-the-art surgery where the entire visceral fascia is removed, was not totally expected. It is also somewhat unusual that it held for all stages, including stage I and II lesions. Unfortunately, despite the benefit shown from preoperative RT, the results will not be directly applicable to therapy in the United States because we do not abide by the short-course schedule for 2 practical reasons. First, as mentioned above, there is no potential for downstaging and therefore little satisfaction realized by treating locally advanced and/or low-lying lesions. Second, morbidity, like acute lumbosacral plexopathy during and after short-course preoperative RT as reported by Frykholm in a follow-up study from Sweden, is much more apt to occur when large fraction sizes are used.[6] In addition, RT here is typically administered concomitantly with chemotherapy either before or after surgery for transmural and/or node-positive lesions, and chemotherapy was expressly forbidden in the Dutch trial.

The 97.6% local control rate for the combined modality arm in the Dutch trial is much better than the 87% local control rate in the previous Swedish trial, which may be attributable to an improvement in surgical technique.[1] The Dutch trial results are similar to the recent early results reported from the NSABP R-03 randomized trial, which also showed better disease-free survival in the preoperative-RT arm.[7] We will have to wait until data from both trials mature in order to determine whether TME is worthwhile, and whether overall survival is indeed improved with preoperative adjuvant RT. ❖

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Sequential Combination Chemotherapy in Patients with Advanced Nonsmall Cell Lung Carcinoma

ABSTRACT & COMMENTARY

Synopsis: Doublet chemotherapy has been associated with median survivals of 8-10 months and 1-year survivals of 30-35% in good performance status patients with advanced nonsmall cell lung cancer (NSCLC). Toxicity has often limited the duration of treatment and the exploration of more aggressive 3-drug regimens due to overlapping toxicities and the frequent presence of multiple comorbid conditions in this patient population. This report explores the use of a sequential chemotherapy regimen that uses a combination of carboplatin and gemcitabine for 3 cycles followed by 3 cycles of paclitaxel. After 6 cycles of treatment, patients were followed without active therapy until disease progression at which time selection of further treatment was at the discretion of the investigator. Even though 27% of patients had a performance status of 2, the regimen was generally well tolerated. There were 2 CRs and 8 PRs in 37 patients with stage IIIB (pleural effusions) (19%) and IV (81%) lung cancer (response rate 27%). Median, 1-year and 2-year survivals for all patients were 9.5 months, 36%, and 11%, respectively. This regimen is currently being compared to standard regimens in a cooperative group trial and represents a possible alternative for patients with poorer performance status.

Source: Edelman M, et al. *Cancer*. 2001;92:146-152.

Recent advances in chemotherapy have extended the median survival of patients with advanced lung cancer from 4-6 months to 8-10 months with 1-year survivals of 30-35%. These studies are, however, heavily influenced by patient selection. Recognizing that chemotherapy is often poorly tolerated in patients with significant comorbid conditions, entry onto clinical trials has typically been restricted to patients who are fully ambulatory (performance status [PS] 0 or 1). In addition, some trials have included patients with stage III disease without pleural effusions, a group that is known to respond better to chemotherapy. Edelman and associates treated 37 patients with NSCLC, 81% of whom had stage IV disease and the remainder with Stage IIIB with pleural effusions with a planned sequential chemotherapy regimen. Patients initially received carboplatin AUC 5.5 day 1 and gemcitabine 1000 mg/m^2 days 1 and 8 every 21 days for 3 cycles followed by paclitaxel 225 mg/m^2 every 21 days for 3 cycles.

In general, therapy was well tolerated. Eighteen patients received all 6 cycles of treatment. Thrombocytopenia was common on day 15 of the carboplatin/gemcitabine regimen but recovery typically occurred by day 21. Grade 4 neutropenia occurred in 21% of patients and in 9% of the cycles; however, febrile neutropenia occurred in only 1% of the cycles and only 3 patients received colony stimulating factors in subsequent cycles. One patient died with complete heart block, possibly related to paclitaxel. Dose reductions or delays, all due to myelosuppression, were required in 17% of the gemcitabine/carboplatin cycles and in 5% of the paclitaxel cycles. Toxicity in patients with PS of 2 was similar to that of the overall study population.

All 37 patients had completed therapy at the time of the report and were evaluable for survival with a median follow-up of 23.5 months. The median survival of the entire population was 9.5 months with 1- and 2-year survivals of 36% and 11%. The median survivals for patients with a PS of 0-1, PS of 2 and those with IIIB disease were 11.2, 6.4, and 15.6 months, respectively.

COMMENT BY MICHAEL J. HAWKINS, MD

While controlled clinical trials understandably restrict eligibility to patients with good performance status, most patients with advanced NSCLC have numerous comorbid illnesses that often prevent aggressive chemotherapeutic approaches. Although a significant number of patients with a PS of 2 were entered and most patients had stage IV disease, the reported regimen produced response rates and survivals similar to those reported in other studies of NSCLC. However, the regimen appeared to be well tolerated and toxicity was primarily limited to myelosuppression; neurotoxicity, often dose limiting following repeated cycles of a platinum/taxane combinations, was not a major problem in this study. This regimen can be considered as a reasonable alternative for patients with poor performance status who wish to be treated for their lung cancer and who are not eligible for a clinical trial. ❖

Potency After Permanent Prostate Implant for Cancer and Androgen Suppression

ABSTRACT & COMMENTARY

Synopsis: The use of implantable iodine-125 or palladium-103 seeds for prostate cancer has increased as biochemical cure rates have been shown to be comparable to those after surgery or external beam radiotherapy. Patients are becoming increasingly aware of the toxicity profiles of the various therapeutic modalities, and may use them as the determining factors in treatment selection. This study, from a Memorial-Sloan Kettering affiliate center, studied an important quality-of-life issue, potency outcomes, in the largest prospective study to date. They showed that the highest 5-year actuarial rate of potency preservation, 76%, occurred in patients treated with seeds alone, while the lowest rate, 29%, was seen in patients subjected to trimodality therapy with a combination of seeds, hormone ablative therapy, and external beam radiotherapy.

Source: Potters L, et al. *Int J Radiat Oncol Biol Phys.* 2001;50:1235-1242.

Prior to seed therapy for localized prostate cancer, a sexual history was obtained from 1166 consecutive patients seen at a MSKCC affiliate center between September 1992 and September 1999. All patients had T1b-T2b disease. Based on inquiries regarding potency status, it was determined that 41% of patients were potent (n = 482). Potency was defined as the ability to achieve an erection sufficient for intercourse without the use of any device or medication. More than half of men > 70 years were impotent, and almost one-third of men 50-55 years were impotent. The potent men were selected to study the impact of therapy on their potency status. The median PSA for the study group was 8, and median patient age was 68 years (range, 49-81 years).

Patients were treated with either iodine-125 or palladium-103 seeds alone, seeds and external beam radiotherapy, or trimodality therapy with the addition of androgen ablation. Brachytherapy and external beam therapy techniques and doses were standard. Patients received seeds alone if their PSA was < 10 and their Gleason score was < 6. All other patients received 41.4-45 Gy 4-field external beam therapy prior to seed implantation per the American Brachytherapy Society guidelines. The 126 patients whose prostates exceeded 60cc in volume (26%) received a median of 4.2 months (range, 1.2-9.5 months) of neoadjuvant hormonal therapy in order to shrink their glands to make implantation feasible. Follow-up was performed in the clinic or by contacting the patient. Median follow-up was 34 months (range, 6-92 months). Potency status for analysis purposes was based on status at the time of the last follow-up visit.

The 5-year actuarial potency status for the entire group was 53%. The patients who did the best were those treated with seeds alone (n = 246, 51%). Their rate of potency preservation was 76%. This was significantly better than for patients treated with seeds preceded by hormone ablative therapy, where 5-year actuarial potency was 52% (P = .0001). It was also better than potency preservation in patients who received a combination of external beam radiotherapy and seeds without hormones (56%), but not statistically significantly better (P = .08). There was no statistically significant difference in potency status between the latter group and patients treated with all 3 modalities (29%, P = .48), although patients given maximal therapy did the worst. A comparison of potency status for patients receiving seeds and hormones did not show a significant difference vs. patients getting seeds, external beam RT, and hormones (P = .13).

Cox proportional hazards analysis of the results showed that age (P = .0001) and use of hormones (P = .04) were significantly related to loss of potency following implantation, while use of external beam radiotherapy was not (P = .11). Among patients who became impotent following therapy, 62% (52/84) responded to silfenadil (Viagra®), including 83% (30/36) of patients who did not receive hormone therapy, and 46% (22/48) of those who did.

Potters et al concluded that hormonal therapy compromises what would otherwise be attractive potency rates in those patients treated with seed implantation. They cited their own retrospective work showing a lack of improvement in biochemical cure rates by the addition of hormone therapy and/or external beam therapy as a rationale to avoid stacking those therapies.[1] They further cited the lack of randomized data supporting combination therapy as a reason to avoid it.

COMMENT BY EDWARD J. KAPLAN, MD

This study confirmed that more therapy means more side effects. The use of hormones had a tremendous impact on patients' potency status in this report. While external beam therapy was added

to the treatment plan for patients with high-risk features (ie, PSA > 10 or Gleason score > 6) the goal of using hormones was to shrink prostates that were considered to be too large to implant. Therefore, as long as size is a barrier to implanting prostates, it becomes difficult to do without hormones. The group that was least affected by the addition of hormones was men < 60 years, who suffered a 24% drop in potency when hormones were added to seeds. This drop increased to 37% if external beam therapy was added. The group that was hurt the most in terms of potency status was men > 70 years. Their potency rate dropped 50% when hormones were added, and it dropped 80% compared to seeds alone if trimodality therapy was used.

Ultimately, the impact of potency enhancers on impotence should not be ignored. Overall, if one considers the 52/84 impotent patients whose potency was restored via silfenadil, 75% of the patients in Potters's study were potent post-treatment. A closer examination shows that nonhormone users did significantly better than hormone users in regaining lost potency (83% vs 46%; $P = .04$).

Although the mechanism for induction of impotence by radiation therapy is not clear, it has been shown that impotence can be reversed with medication. This becomes much more difficult to achieve if hormones are used, and is difficult to justify if no survival benefit associated with hormone use can be demonstrated. Until randomized study data have been reported, men who are contemplating seed implantation must be made aware of the potential long-term effect of hormone therapy on their quality of life. ❖

Reference

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CME Questions

16. Which one of the following statements regarding metastatic non-small cell carcinoma of the lung is *not* true?

a. Approximately one-third of patients with a good performance status can be expected to have objective responses to chemotherapy.
b. Approximately one-third of patients with a good performance status can be expected to be alive after 1 year.
c. Survival for Stage IIIB patients with pleural effusions is comparable to that of Stage IV patients.
d. Survival is frequently affected by the presence of co-morbid conditions.

17. Patients with peritoneal carcinomatosis from colorectal primary tumors:

a. invariably will die from their metastatic cancer within 5 years.
b. may be rendered disease free for 5 years following aggressive surgical debulking and intraperitoneal chemotherapy.
c. aggressive surgical debulking and intraperitoneal chemotherapy is well tolerated with minimal postoperative mortality and a low incidence of re-resection.
d. warrant aggressive intraperitoneal surgery and chemotherapy even in the presence of disease outside of the peritoneal cavity.

18. In the Dutch Colorectal Cancer Group trial:

a. the researchers anticipate that an overall survival benefit will become apparent as follow-up data are tallied.
b. only node-positive patients benefited from preoperative adjuvant therapy.
c. there were significantly more postoperative deaths in the combined modality arm vs. the surgery alone arm.
d. total mesorectal excision achieved local control rates comparable to those achieved in the combined modality arm.

19. Short-course preoperative radiotherapy is associated with all of the following *except*:

a. a higher local control rate vs. surgery alone.
b. acute lumbosacral plexopathies.
c. a higher overall survival rate vs. surgery alone.
d. the ability to effectively downstage rectal cancers.

20. Which of the following statements is *false* about the association of ulceration and melanoma?

a. It is the second most important prognostic factor behind tumor thickness in predicting survival in primary melanoma.
b. It is more important than level of invasion for melanomas greater than 1.0 mm
c. It remains an important prognostic variable even for patients with stage III disease.
d. It remains an important prognostic variable even for patients with stage IV disease.

21. Which of the following factors had a statistically significant impact on potency in Potter et al's study?

a. Patient age
b. Use of hormonal therapy
c. a and b
d. None of the above

Readers are Invited. . .

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In Future Issues:

Survival Following Induction Chemoradiotherapy and Esophagectomy for Esophageal Carcinoma