Treatment Failure After Primary and Salvage Therapy for Prostate Cancer

Likelihood, Patterns of Care, and Outcomes

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BACKGROUND. The authors report the likelihood of treatment failure and the outcomes after salvage therapy among men with prostate cancer who initially either received external-beam radiation therapy (EBRT) or underwent radical prostatectomy (RP).

METHODS. Using a national disease registry, the Cancer of the Prostate Strategic Urological Research Endeavor (CaPSURE) database, 5277 men with prostate cancer were identified who initially either underwent RP (4342 men) or received EBRT (935 men). Outcomes after disease recurrence and subsequent salvage therapy were assessed.

RESULTS. Recurrent disease developed in 1590 men (30%), including 1003 patients (23%) in the RP group and 587 patients (63%) in the EBRT group, at a mean of 34 months and 38 months, respectively (P = .003). Patients who had recurrent disease had greater rates of overall death (19% vs 3%; P < .01) and bone metastases (15% vs 1%; P < .01). Data after salvage therapy were available for 1050 patients (620 men in the RP group and 430 men in the EBRT group). Androgen-deprivation therapy (ADT) was the most common salvage treatment in both groups. Overall, 420 men in the RP group (68%) and 319 men in the EBRT group (74%) failed salvage therapy at mean of 43.6 months and 43.8 months, respectively (P = .95). These patients had a greater overall death rate than the 311 patients who did not fail salvage therapy (24.8% vs 6.9%, respectively; P < .001). No survival benefit in terms of prostate cancer-related death (P = .91) was identified with any particular combination of primary and salvage therapy.

CONCLUSIONS. Disease recurrence developed in 30% of patients who were treated for prostate cancer, and ADT was the most common salvage therapy used. Patients who failed salvage therapy had worse overall survival, and no survival benefit was noted for any particular combination of primary and salvage therapy.


KEYWORDS: androgen-deprivation therapy, outcome assessment, prostatic neoplasms, salvage therapy.

Prostate cancer is the most common cancer diagnosed among American men. Because of widespread screening and early detection efforts, stage migration has occurred, and tumor classification 1c (T1c) disease now accounts for the most common clinical presentation of prostate cancer.1 The majority of these patients are well suited for localized and curative therapy. Radical prostatectomy (RP) and external-beam radiation therapy (EBRT) represent the most common treatment options for men with clinically localized prostate cancer. Regardless of their primary treatment, approximately 12% to 42% of men who undergo RP2 and approximately
22% to 69% of men who receive EBRT will develop biochemical recurrence (BCR), which most often precedes clinical recurrence by years.

The treatment of recurrent disease poses a clinical challenge. Recurrence must be identified as local or distant, and secondary or salvage treatment should be tailored specifically. Ideally, treatment should address the recurrent disease without compromising quality of life. Because to our knowledge no specific guidelines regarding salvage therapy exist, most practitioners treat according to their clinical judgment, experience, and local practice patterns. Most important, the ultimate outcomes after administering salvage therapy are extremely variable, and it is unknown whether or not salvage therapy has an important impact on cause-specific survival.

The Cancer of the Prostate Strategic Urological Research Endeavor (CaPSURE) database has been used previously to describe patterns of use of second treatment after local therapy for prostate cancer. The objectives of this article were to update the previously published data and to describe further the natural history of patients undergoing salvage therapy. We sought to determine national trends in the use of primary and salvage therapy and the outcomes of these treatments by analyzing this large, multi-institutional, prostate cancer database. We also attempted to identify risk factors that determined the likelihood of disease recurrence and salvage treatment success. Finally, we also assessed the outcomes of men who failed salvage therapy.

MATERIALS AND METHODS

CaPSURE is a longitudinal registry of men with prostate cancer who were recruited from 31 community and academic urology practices throughout the U.S. Clinical, treatment, quality of life, sociodemographic, and outcome information is tracked longitudinally. Patients are followed until death or withdrawal. Additional details on the information recorded and the methodology of obtaining the data have been published previously.

At the time of the current analysis, 12,005 patients with prostate cancer diagnosed between 1989 and 2004 were identified. Among them, 5277 patients underwent primary therapy with either RP or EBRT and received either a second form of treatment or ample prostate-specific antigen (PSA) data on follow-up to assess accurately for failure. Failure or disease recurrence was defined as 2 consecutive increases in serum PSA from a postirradiation nadir PSA. In addition, men who received a second form of treatment ≥6 months after primary treatment were considered to have failed. Patients were stratified into pretreatment clinical risk groups based on 1992 American Joint Commission on Cancer clinical stage, serum PSA at diagnosis, and Gleason biopsy grade according to the classification system of D’Amico et al. All patients who had recurrent disease and underwent secondary therapy were identified, and differences in survival between patients who did and did not develop recurrent disease after salvage therapy were assessed using chi-square analysis and analysis of variance. In addition, patients were assessed to determine whether any differences in outcome emerged based on a particular combination of primary and salvage treatments.

RESULTS

Of the 5277 patients who underwent primary therapy with RP or EBRT, 4342 underwent RP, and 935 received EBRT. Radiation therapy consisted of EBRT only, although the exact details of the radiation administration were not known for each site or for each patient. The clinical characteristics of these 2 groups based on initial treatment are summarized in Table 1. The 2 groups differed significantly (P < .01) in their age at diagnosis, the percent of positive biopsies obtained, PSA level at diagnosis, clinical tumor classification (T classification) on diagnosis, Gleason grade on biopsy, and pretreatment clinical risk status. In general, patients who received EBRT as primary treatment were much older than patients who underwent primary RP: Twenty-seven percent of patients were aged ≥75 years in the EBRT group compared with 2% in the RP group. In addition, these patients had higher serum PSA levels at diagnosis with: Fifty percent of patients in the EBRT group had a PSA level >10 ng/mL compared with only 21% in the RP group. Finally, 45% of patients in the EBRT group were classified with high-risk disease compared with only 19% in the RP group.

Overall, recurrent disease developed in 1590 patients (30% of 5277 patients), including 1003 patients (23%) in the RP group and 587 patients (63%) in the EBRT group. Recurrent disease was identified by PSA criteria in 804 patients (51%) and by second treatment criteria in 786 patients (49%). The mean time between primary treatment and recurrence was 34 months in the RP group and 38 months in the EBRT group (P = .003). The clinical
characteristics of patients who had recurrent disease and had data available regarding secondary salvage therapy (n = 1050 patients) versus patients who did not have recurrent disease (n = 3683 patients) are summarized in Table 2. Patients who did and did not develop recurrent disease differed significantly in all characteristics that were analyzed (P < .01): They were older, had higher mean serum PSA levels at diagnosis (10.3 ng/mL vs 5.8 ng/mL), and presented with more advanced disease at presentation based on clinical T classification and Gleason score. The patients with recurrent disease had more frequent bone metastases (15% vs 1%; P < .01), increased overall mortality (19% vs 3%; P < .01), and increased prostate cancer-specific mortality (45% vs 0%; P < .01). Of the patients who had surgical margin data available (n = 4101 patients), 29.1% had positive margins. Among those patients, 37.6% developed recurrent disease. Among the patients who had recurrent disease, 53.3% had positive margins, whereas only 23% of patients without recurrent disease had positive margins (P < .01).

Multivariate analysis of the predictors of BCR after primary RP demonstrated that the following factors were independent predictors of BCR: age at diagnosis, PSA at diagnosis, clinical T classification, Gleason score, bone metastases, overall survival, and prostate cancer-related death.
variables were associated significantly: Gleason grade on biopsy ($P = .0001$), pathologic Gleason grade ($P < .0001$), pathologic T classification ($P < .0001$), risk factor group ($P < .0001$), surgical margin status ($P < .0001$), and adjuvant and/or neoadjuvant therapy ($P = .0347$). Increasing Gleason grades on biopsy and prostatectomy specimens and increasing pathologic T classification were correlated with a higher likelihood of BCR. Compared with the low-risk group (defined using criteria published by D’Amico et al.), patients in the intermediate-risk group (odds ratio [OR], 0.550; 95% confidence interval [95% CI], 0.391–0.773) and the high-risk group (OR, 0.210; 95% CI, 0.136–0.323) had a lower likelihood of BCR-free survival. Patients with negative surgical margins had a lower likelihood of BCR-free survival (OR, 2.840; 95% CI, 1.597–5.049). Positive surgical margins were associated with a higher likelihood of BCR (OR, 1.107; 95% CI, 0.619–1.979) compared with unknown margin status. The use of adjuvant and/or neoadjuvant therapy was a predictor of BCR on multivariate analysis. Subgroup analysis revealed that the use of adjuvant therapy (OR, 0.563; 95% CI, 0.241–1.314), neoadjuvant therapy (OR, 0.603; 95% CI, 0.387–0.941), or a combination of adjuvant and neoadjuvant therapy (OR, 0.656; 95% CI, 0.420–1.025) did not result in a lower likelihood of BCR.

A multivariate model of the predictors of BCR after primary EBRT revealed that the only significant variables were risk group ($P < .0001$) and adjuvant and/or neoadjuvant therapy ($P < .0001$). Compared with the low-risk group, patients in the intermediate-risk group (OR, 0.283; 95% CI, 0.176–0.455) and the high-risk group (OR, 0.092; 95% CI, 0.056–0.152) had a decreased likelihood of BCR-free survival. Unlike patients who had BCR after primary RP, the use of adjuvant and/or neoadjuvant therapy in patients who received primary EBRT protected against BCR. However, only the use of adjuvant therapy (OR, 2.822; 95% CI, 1.652–4.822) and a combination of adjuvant and neoadjuvant therapy (OR, 3.648; 95% CI, 2.442–5.448) protected against BCR. The use of neoadjuvant therapy alone did not protect against BCR (OR, 0.591; 95% CI, 0.198–1.765).

Among the 1003 patients who initially underwent RP and subsequently developed recurrent disease, 785 patients (78%) did not receive adjuvant or neoadjuvant therapy. Among the patients who did receive adjuvant and/or neoadjuvant therapy, 31 patients (3%) received an unspecified combination of neoadjuvant and adjuvant therapy. Patients who received adjuvant and/or neoadjuvant therapy had higher Gleason grades on biopsy and a higher rate of bone metastases (13% vs 8%; $P = .02$). The use of adjuvant and/or neoadjuvant therapy ultimately did not have an impact on overall survival ($P = .27$).

Among the 587 patients who initially received EBRT and developed recurrent disease, 356 patients (61%) did not receive adjuvant or neoadjuvant therapy. Among the patients who did receive adjuvant and/or neoadjuvant therapy, 148 patients (25%) received neoadjuvant and adjuvant ADT, 24 patients (4%) received neoadjuvant ADT, 57 patients (9.7%) received neoadjuvant androgen therapy, and 2 patients (0.3%) received an unspecified combination of neoadjuvant and adjuvant therapy. Patients who received adjuvant and/or neoadjuvant therapy had a higher mean serum PSA level at diagnosis (54 ng/mL vs 23 ng/mL) than patients who did not receive any additional therapy. The use of adjuvant and/or neoadjuvant therapy improved overall survival (83% vs 68%; $P < .01$) compared with not receiving such therapy.

A multivariate regression analysis was performed in all patients to determine which factors predicted the use of adjuvant and/or neoadjuvant therapy. The effect of variables was assessed individually on adjuvant, neoadjuvant, and combination therapies. Variables for which this analysis was adjusted included initial treatment type (RP or EBRT), clinical risk category at diagnosis, age, education, race, income, and number of comorbidities. Only risk group ($P < .0001$) and race ($P = .0322$) were predictive of the use of adjuvant and/or neoadjuvant therapy in patients who initially underwent RP. Compared with being in the low-risk group, being in the high-risk group predicted the use of adjuvant therapy (OR, 1.582; 95% CI, 1.398–3.301), neoadjuvant therapy (OR, 5.617; 95% CI, 3.427–9.206), and a combination of both therapies (OR, 8.863; 95% CI, 5.461–14.384). Compared with white RP patients, RP patients of other races were less likely to receive adjuvant therapy (OR, 0.698; 95% CI, 0.249–1.957) or combination therapies (OR, 0.388; 95% CI, 0.178–0.847) but were more likely to receive neoadjuvant therapy (OR, 1.459; 95% CI, 0.880–2.418). The only significant predictor of adjuvant and/or neoadjuvant therapy in patients who initially received EBRT was clinical risk group ($P = .0016$). Compared with being in the low-risk group, being in the high-risk group predicted the use of adjuvant therapy (OR, 1.295; 95% CI, 0.553–3.032), neoadjuvant therapy (OR, 1.840; 95% CI,
Of the 1590 patients who developed recurrent disease, 70.5% were treated at a mean of 40.2 months. PSA data after salvage therapy was available in 1050 patients (620 patients who underwent initial RP and 430 patients who received initial EBRT). The most common salvage treatment employed in both groups was ADT in 367 of 620 patients (59.2%) in the RP group and 402 of 430 patients (93.5%) in the EBRT group. The second most common salvage treatments employed were EBRT in 248 of 620 patients (40%) in the RP group and cryotherapy in 13 of 430 patients (3%) in the EBRT group. The remaining forms of salvage therapy are listed in Table 3.

Failure after salvage therapy was defined as the presence of detectable PSA (>0.2 ng/mL) after treatment. Overall, 420 of 620 patients (68%) in the RP group and 319 of 430 patients (74%) in the EBRT group failed salvage therapy, because they had a postsalvage therapy serum PSA level >0.2 ng/mL. Among these 739 patients who failed salvage therapy, 24.8% died compared with only 6.9% of the 311 patients with adequate PSA data after salvage therapy who did not fail salvage therapy. The mean survival for those who failed was 81.1 months (median, 59.9 months) as opposed to a mean survival of 103.2 months (median, 101.2 months) for those who did not fail. This difference in overall survival was statistically significant (\(P < .001\)).

The mean values of the first detectable serum PSA after salvage therapy were 0.65 ng/mL for the entire RP group and 0.74 ng/mL for the entire EBRT group (\(P = .95\)). The time from the initiation of salvage treatment to the first detectable PSA did not differ between the RP and EBRT groups (RP group: mean, 43.6 months; median, 33.1 months; EBRT group: mean, 43.8 months; median, 36.9 months; \(P = .95\)). Subset analyses within the EBRT group revealed that groups treated with some form of neoadjuvant and/or adjuvant therapy had a shorter mean time to PSA recurrence after salvage therapy (range, 30–38 months; median, 22.3 months) compared with the group that received no neoadjuvant or adjuvant ADT (mean, 47 months; median, 40.2 months). This difference in the mean time to PSA recurrence was statistically significant (\(P < .001\)).

Finally, no survival benefit for prostate cancer-related death was identified for any particular combination or strategy of initial and salvage treatment. No statistically significant difference in prostate cancer-related death rates (\(P = .71\)) was observed between patients in the RP group who received salvage EBRT as opposed to salvage ADT (42% vs 47%, respectively). No meaningful comparison between differences in prostate cancer-related death rates among different salvage therapies used in patients who received primary EBRT could be performed, because the majority of those patients received ADT (93.5%) whereas only a handful (6%) received potentially curative therapies. However, all patients who did not fail salvage therapy, as defined by a postsalvage treatment PSA level <0.2 ng/mL, had an improved overall survival rate compared with the patients who did fail salvage therapy. Among the 739 patients with PSA data after salvage therapy who failed such therapy, approximately 46% of the 70 deaths in the salvage group that initially underwent RP were related to prostate cancer versus 45% of the 96 deaths in the salvage group that initially received EBRT (\(P = .91\)).

**DISCUSSION**

Despite early detection efforts and the resulting stage migration in prostate cancer treatment, disease recurrences still develop in a significant proportion of patients after EBRT or RP. The natural history of those who fail after surgery or EBRT is a matter of much interest and debate. Research suggests that BCR as defined by a single PSA value may not be a valid clinical endpoint, because measures of PSA kinetics, PSA doubling time after primary therapy, and PSA velocity prior to primary treatment may be better predictors of prostate cancer recurrence and/or survival. Furthermore, the overall survival rate at 10 years was the same for patients with and without BCR. However, the results of the current study do not corroborate this finding, because as we observed higher rates of death in patients who developed recurrent disease compared with those patients who did not (19% vs 3%; \(P < .01\)), and up to 45% of the deaths in the group with BCR were related to pros-

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**TABLE 3**

<table>
<thead>
<tr>
<th>Salvage therapy</th>
<th>Primary RP (N = 620)</th>
<th>Primary EBRT (N = 430)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Androgen deprivation</td>
<td>367 (59.2)</td>
<td>402 (93.5)</td>
</tr>
<tr>
<td>EBRT</td>
<td>248 (40.0)</td>
<td>8 (1.9)</td>
</tr>
<tr>
<td>Cryotherapy</td>
<td>3 (0.5)</td>
<td>13 (3.0)</td>
</tr>
<tr>
<td>Radical prostatectomy</td>
<td>NA</td>
<td>4 (0.9)</td>
</tr>
<tr>
<td>Brachytherapy</td>
<td>NA</td>
<td>1 (0.2)</td>
</tr>
<tr>
<td>Unknown</td>
<td>2 (0.3)</td>
<td>2 (0.5)</td>
</tr>
</tbody>
</table>

RP indicates radical prostatectomy; EBRT, external-beam radiation therapy; NA, not applicable.
tate cancer compared with none of the deaths in the group without BCR (Table 2).

In the current study, the mean time between primary treatment and recurrence was 34 months in the RP group and 38 months in the EBRT group ($P = .003$). Although there was a statistical difference in the mean times, the difference of 4 months may not be meaningful clinically, because the definitions of BCR are different for these 2 groups. The rate of recurrence after RP reported herein (23%) was consistent with the rates reported in other contemporary series (range, 15%–33%). The rate of recurrence among patients in the EBRT group in the current study (63%) was slightly higher than the rates reported by others (from 37% to 48%). However, the recurrence rate in our series was similar to that observed by D’Amico et al., who reported 5-year BCR rates from 16% to 57% among patients who received EBRT without adjuvant ADT.

Neoadjuvant and/or adjuvant ADT was not delivered routinely to all men with intermediate- and high-risk disease features; however, in the multivariate analysis, clinical risk group was the most important predictor of the delivery of such therapy for all patients. Patients with high-risk clinical features were more likely to receive combination adjuvant and neoadjuvant therapy than either therapy alone. An odd finding of the study was that race was a predictor of the use of adjuvant and/or neoadjuvant therapies on multivariate analysis in patients who initially underwent RP only. Non-Caucasians were more likely to receive neoadjuvant therapy but were less likely to receive adjuvant and combination therapies. These results are difficult to explain and may be tied into other factors, such as education, income, patient compliance, and health care access. For example, neoadjuvant therapy may be easier to deliver in patients with little economic means and a history of poor compliance compared with delivering prolonged courses of adjuvant or combination therapy. Unfortunately, such socioeconomic data were not available for all patients; thus, the effects of these variables were not factored adequately into the multivariate model.

We observed mixed results with the use of neoadjuvant and/or adjuvant therapy in the current study. In patients who initially underwent RP, the use of such therapies did not protect against disease recurrence. Results of randomized trials, however, suggest that such combination treatment decreases BCR rates in patients who receive EBRT. In our study, the use of neoadjuvant and/or adjuvant therapy protected against BCR and resulted in improved overall survival (83% vs 68%; $P < .01$) in patients who initially received EBRT; however, in the subset of patients that subsequently went on to receive salvage therapy, the time to biochemical failure was shorter (30–38 months vs 47 months; $P < .001$). This difference may have occurred because the patients who received neoadjuvant/adjuvant therapy did so at the expense of delayed primary and secondary therapy, which may explain the shorter time to PSA recurrence. However, the additional therapy may have translated into a slight advantage in overall survival.

Nevertheless, the high recurrence rate among the patients who received initial EBRT in our study may have been caused by the presence of high-risk pretreatment clinical features in 45% of those who received initial EBRT. This phenomenon is reflected by the high use of neoadjuvant and/or adjuvant therapy in these patients (39% of patients in the EBRT group). Furthermore, because these patients were accrued from many different practices from as early as 1989, radiation dosing may have been suboptimal in terms of dose delivery, fields of treatment, and methods of administration. Unfortunately, the CaPSURE database does not contain detailed information regarding EBRT to explore this issue further.

The main focus of the current study was to determine the types and outcomes of salvage therapies used in patients who developed recurrent disease. Among the 1590 patients who had recurrences, PSA data were available for 1050 patients (620 patients in the RP group and 430 patients in the EBRT group) to assess for the response to salvage therapies. The most common form of secondary or salvage therapy used in both groups was ADT, which was administered in 59.2% of patients in the RP group and 93.5% of patients in the EBRT group. Serum PSA values decreased after salvage therapy to undetectable levels, and failure after salvage therapy was defined as the presence of a postsalvage therapy serum PSA level $>0.2$ ng/mL. According to this definition, 739 patients (68% of 620 patients in the RP group and 74% of 430 patients in the EBRT group) failed salvage therapy. Almost 25% of these patients died compared with only 6.9% of the remaining 311 patients who did not fail salvage therapy, and this difference was statistically significant ($P < .001$).

The definition of failure after salvage therapy has not been well established. We defined failure as the presence of a detectable serum PSA level ($>0.2$ ng/mL) by extrapolating from the definition of failure after primary prostatectomy. The finding that patients who failed salvage therapy had decreased overall survival compared with patients who did not fail corroborates this arbitrary definition. A recent
report defined progression of disease after salvage EBRT as a serum PSA level >0.1 ng/mL in patients with BCR after primary RP. According to this definition, 30% of patients had disease progression in our series. Although this rate is markedly lower than our overall failure rates after salvage therapy, approximately 92% of the patients reported by Terai et al. had PSA levels <0.5 ng/mL before salvage EBRT was initiated.15 Stephenson et al. defined failure after salvage EBRT for BCR after primary RP as a serum PSA level >0.1 ng/mL above the postradiotherapy PSA nadir; those authors determined that disease progression occurs in approximately 50% of patients, and distant metastases occurs in another 10% of patients.16 These results are more comparable to the 68% salvage therapy failure rate in our patients who initially underwent RP. These patients may have fared slightly worse than the multicenter-derived cohort in the study by Stephenson et al., because only 40% of them received salvage EBRT. Nevertheless, no statistically significant benefit in prostate cancer-related survival was noted for patients who received salvage EBRT versus salvage ADT.

Our results did not demonstrate a survival benefit (P = .91) for any particular combination of initial and salvage treatments. Failure after the administration of any salvage therapy after primary therapy did not occur until a mean of 43.6 months versus 43.8 months (P = .95) with mean serum PSA levels of 0.65 ng/mL and 0.74 ng/mL (P = .95) at the time of recurrence for the initial RP and EBRT groups, respectively. In the 420 patients who failed primary EBRT, only 13 patients (3%) underwent salvage cryotherapy, and only 4 patients (0.9%) underwent salvage prostatectomy. These salvage therapies potentially are curative if they are administered early after recurrence, as demonstrated by several single-institution series. The 20-year experience with salvage RP at the University of Southern California demonstrated 5-year progression-free survival rates of 100% for patients with pathologic T2/lymph node negative (pT2N0) disease and 35% for patients with pT3N0 disease.17 Likewise, salvage cryotherapy has demonstrated a 5-year disease-specific survival rate up to 94% and a 90% disease-free survival rate in patients with small-volume, organ-confined disease (clinical T1/clinical T2) prior to initial therapy.18

There were several limitations to our study. Because this was a retrospective and multistitutional study, potential errors may have been introduced by incomplete data acquisition, patient selection bias, and practice participation bias (only certain practices contribute data to the CaPSURE database). Although we defined conditions in accordance with previously published reports, the lack of uniformity in certain definitions makes our interpretation of the data subject to our definitions. For example, no uniform definition exists for BCR. BCR may have been lower if we had applied a different definition of PSA recurrence after primary therapy. Defining BCR after EBRT is more difficult, especially because its natural history has not been described as well as its natural history after RP. We defined post-EBRT BCR according to the ASTRO definition of BCR after EBRT. This definition backdates the date of failure or BCR to the point in time that is midway between the postirradiation nadir PSA and the first of the 3 consecutive serum PSA rises. Unfortunately, the ASTRO definition is plagued by biases, including lack of concordance with BCR definitions after RP and artificially improved recurrence rates based on backdating errors. In fact, a recent multi-institutional pooled analysis demonstrated that alternate BCR definitions have higher sensitivity and specificity than the ASTRO definition for predicting clinical and distant failure after primary treatment with EBRT.19 Although we recognize the inherent flaws in the ASTRO definition, we still chose to use it; because, currently, it remains the most popular definition for BCR after EBRT, and it also is consistent with previous CaPSURE reports. Finally, as this report demonstrates, the use of potentially curative salvage therapies for recurrent prostate cancer are being underused greatly by the majority of practices across the U.S. Consequently, our conclusion that there is a lack of survival benefit with a particular combination of primary and salvage treatment must be interpreted with the caveat that the majority of patients received noncurative salvage therapy in the form of ADT. Despite these limitations, the data presented provide reasonably accurate insight into urologic practice and outcomes across the country.

The results of the current study demonstrate that, despite intense prostate cancer screening and substantial stage migration, approximately 30% of men with prostate cancer still fail primary therapy. The risk of failure correlates with traditional predictors of tumor aggressiveness, including Gleason grade at biopsy, clinical stage, and pretreatment serum PSA level. The use of neoadjuvant and/or adjuvant therapies at the time of primary treatment resulted in decreased rates of bone metastases and improved overall survival in the group that initially received EBRT. However, the use of such therapies did not shorten the mean time to PSA recurrence. The most common additional salvage therapy that was used after failure with either RP or EBRT was ADT. Unfortunately, most patients failed salvage ther-
apy; and the patients who did fail salvage therapy were more likely to die of their disease. However, response to salvage therapy appeared to be similar for patients who were treated with either primary therapy, and no survival benefit for a particular combination of primary and salvage therapy was demonstrated during the limited follow-up period.

REFERENCES


