UROLOGICAL ONCOLOGY

Androgen suppression adjuvant to definitive radiotherapy in prostate carcinoma – long-term results of phase III RTOG 85-31

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Purpose: Radiation Therapy Oncology Group protocol 85-31 was designed to evaluate the effectiveness of adjuvant androgen suppression, using goserelin, in unfavorable prognosis carcinoma of the prostate treated with definitive radiotherapy (RT).

Methods and Materials: Eligible patients were those with palpable primary tumor extending beyond the prostate (clinical Stage T3) or those with regional lymphatic involvement. Patients who had undergone prostatectomy were eligible if penetration through the prostatic capsule to the margin of resection and/or seminal vesicle involvement was documented histologically. Stratification was based on histologic differentiation, nodal status, acid phosphatase status, and prior prostatectomy. The patients were randomized to either RT and adjuvant goserelin (Arm I) or RT alone followed by observation and application of goserelin at relapse (Arm II). In Arm I, the drug was to be started during the last week of RT and was to be continued indefinitely or until signs of progression.

Results: Between 1987 and 1992, when the study was closed, 977 patients were entered: 488 to Arm I and 489 to Arm II. As of July 2003, the median follow-up for all patients was 7.6 years and for living patients was 11 years. At 10 years, the absolute survival rate was significantly greater for the adjuvant arm than for the control arm: 49% vs. 39%, respectively ($p = 0.002$). The 10-year local failure rate for the adjuvant arm was 23% vs. 38% for the control arm ($p < 0.0001$). The corresponding 10-year rates for the incidence of distant metastases and disease-specific mortality was 24% vs. 39% ($p < 0.001$) and 16% vs. 22% ($p = 0.0052$), respectively, both in favor of the adjuvant arm.

Conclusion: In a population of patients with unfavorable prognosis carcinoma of the prostate, androgen suppression applied as an adjuvant after definitive RT was associated not only with a reduction in disease progression but in a statistically significant improvement in absolute survival. The improvement in survival appeared preferentially in patients with a Gleason score of 7-10.

Editorial Comment

Androgen suppression adjuvant to radiotherapy is often performed, for better or worse. The long-term sequelae of this therapy e.g. bone demineralization and loss of muscle, are slowly recognized and will be in the focus of a later comment. The advantage of adjuvant therapy especially with regard to survival, however, was disputable. The long-term outcome data of this RTOG trial supports the efficacy of adjuvant hormone therapy.

Briefly, both progression measured as local and distant failure, and survival with or without evidence of disease were statistically significant better in the treatment arm. With regard to Gleason score, the subset of patients with Gleason 8-10 benefited most.

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Monotherapy for stage T1-T2 prostate cancer: radical prostatectomy, external beam radiotherapy, or permanent seed implantation

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Background and Purpose: To review the freedom from biochemical recurrence (FBR) rates after permanent prostate brachytherapy (PPB), external beam radiotherapy (RT) to a minimum 70Gy, or radical prostatectomy (RP) for clinically localized stage T1-T2 adenocarcinoma of the prostate.

Patients and Methods: The study cohort consisted of 1819 consecutively treated clinical stage T1-T2 (AJCC 1997) localized prostate cancer patients between 1992 and 1998. All patients received monotherapy treatment without additional adjuvant therapy. The distribution by treatment modality was as follows: RT for 340, RP for 746, and PPB for 733 cases. The median follow-up time was 58 months for all cases (51 months for PPB cases, 56 months for RT cases, and 64 months for RP cases). Biochemical relapse was defined as to be detectable PSA levels in RP cases, and the ASTRO consensus panel definition for the RT and PPB cases.

Results: The 7-year FBR rates for PPB vs. EBRT vs. RP were 74, 77, and 79%, respectively. Multivariate analysis identified iPSA ($P < 0.001$) and bGS ($P < 0.001$) as independent predictors of relapse. Treatment modality, age, clinical T-stage, and race were not independent predictors of failure.

Conclusions: Pretreatment PSA levels, and biopsy Gleason score determined outcome in this study cohort. Biochemical failure rates in this study cohort are similar between PPB, RT, and RP as monotherapy for clinically localized prostate cancer.

Editorial Comment

Among several treatment options for localized prostate cancer radical prostatectomy is most often performed worldwide. The scientific basis for this , however, is swaying.

This retrospective outcome analysis of data from 1819 patients treated with either radical prostatectomy (RP), external beam radiation therapy (ERBT), or permanent prostate brachytherapy (PPB) deserves interest as it focuses solely on the subgroup of patients without adjuvant or pretreatment hormone therapy, thus, a relatively favorable subgroup of prostate cancer patients.

For all 1819 patients, the overall 7-year PSA progression rates were 76%. The 7-year PSA progression rates for RP, RT and PPB were 79%, 77% and 74% respectively. The multivariate analysis identified only pretreatment PSA and Gleason score as predictors for failure. With other words, first, no treatment fared significantly better than another. Second, there is still room for improvement especially in RT and PPB, as higher doses and better techniques are currently under evaluation here. I would predict that in 10 years from now RP would play an only minor role for the treatment of prostate cancer.

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