Does Short-Term Androgen Deprivation Substitute for Radiation Dose in the Treatment of High Risk Prostate Cancer

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Background

- There are several randomized trials that confirm a clinical and/or biochemical benefit with the use of androgen deprivation (AD) as a component of treatment in high risk prostate cancer, especially when combined with radiotherapy (RT). Studies show AD downsizes the prostate and decreases the PSA through a decrease in proliferation of cancer cells as well as an increase in apoptosis. It is unclear if it acts additively or synergistically with RT to enhance tumor killing. There are also data supporting the escalation of 3D conformal RT dose in patients with localized prostate cancer with an intermediate-high risk of failure. The benefit of dose escalation in low risk (PSA < 10 ng/ml) patients is not clear. This study attempts to determine whether the addition of short-term AD (6 months or less) to 3D conformal RT is an effective substitute for dose escalation in the treatment of high-risk prostate cancer.

Materials and Methods

- 296 patients with high-risk, non-metastatic (PSA>20, Gleason Score [GS] 7-10, and T3/4) prostate cancer were treated with RT alone (n=206) or RT in combination with short-term AD (n=90) between 3/1990 and 11/1998.
- Median patient characteristics were: age of 68 years, follow-up of 58 mo, pretreatment PSA (pre-PSA) of 21.8 ng/ml, RT dose of 75 Gy (range 62-80 Gy), AD duration of 2.9 months (range 1-6 mo), and time off AD of 64 mo. AD was administered neoadjuvantly in 16, concurrently in 4, and neoadjuvantly and concurrently in 70 cases.
- Stepwise Cox proportional hazards regression multivariate analysis (MVA) was performed to determine independent correlates of freedom from biochemical failure using ASTRO consensus guidelines (bNED), distant metastasis (DM), and overall survival (OS).
- The impact of short-term AD with respect to dose was then examined using univariate analysis for dose ranges of < 75Gy (median dose of 71.6 Gy, n=158) and >=75 Gy (median dose of 75.8 Gy, n=138).
- Median follow-up time for both dose groups was similar.
- Matched pair analysis was performed comparing bNED rates for Group A ( < 75 Gy + ST AD) vs Group B (>=75 Gy alone) to determine whether ST AD can substitute for higher dose without compromising long-term biochemical control.

Results

- On MVA, pre-PSA (HR=1.009, p=0.0002) and RT dose (HR=0.581, p=0.003) were significant correlates of bNED.
- For DM and OS, the significant covariates were T-stage (HR=1.067, p=0.02) and GS (HR=1.219, p=0.01), respectively.
- The addition of short course AD did not altered patient outcome significantly on MVA.
- In univariate analyses, the addition of short term AD had no impact on bNED, DM, and OS in either the low dose or high dose group.
- Finally, matched pair analysis (match for T-stage, GS, and pre-PSA) comparing Group A vs. Group B resulted in a significant difference in bNED in favor of the higher dose group (Group A 38% vs Group B 54%, p=0.0069). This was not seen for DM or OS.

Author's Conclusions

- The data suggest that short term AD is not a substitute for RT dose in the treatment of high-risk prostate cancer.
- In both univariate and multivariate analyses, the addition of short term AD provided no additional benefit with respect to
bNED, DM, and OS.

Clinical/Scientific Implications

- This study suggests that RT dose remains an important element in the treatment of high risk prostate cancer.
- However, this appears to be true in terms of biochemical control only since the benefit did not translate into improvements in for DM or OS.
- Long-term follow-up is necessary to determine if this benefit in biochemical control with higher RT doses is clinically relevant.

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