UROLOGICAL ONCOLOGY

Risk of Prostate Cancer-Specific Mortality Following Biochemical Recurrence after Radical Prostatectomy

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Context: The natural history of biochemical recurrence after radical prostatectomy can be long but variable. Better risk assessment models are needed to identify men who are at high risk for prostate cancer death early and who may benefit from aggressive salvage treatment and to identify men who are at low risk for prostate cancer death and can be safely observed.
Objectives: To define risk factors for prostate cancer death following radical prostatectomy and to develop tables to risk stratify for prostate cancer-specific survival.
Design, Setting, and Patients: Retrospective cohort study of 379 men who had undergone radical prostatectomy at an urban tertiary care hospital between 1982 and 2000 and who had a biochemical recurrence and after biochemical failure had at least 2 prostate-specific antigen (PSA) values at least 3 months apart in order to calculate PSA doubling time (PSADT). The mean (SD) follow-up after surgery was 10.3 (4.7) years and median follow-up was 10 years (range, 1-20 years).
Main Outcome Measure: Prostate cancer-specific mortality.
Results: Median survival had not been reached after 16 years of follow-up after biochemical recurrence. Prostate-specific doubling time (< 3.0 vs 3.0-8.9 vs 9.0-14.9 vs > or =15.0 months), pathological Gleason score (< or =7 vs 8-10), and time from surgery to biochemical recurrence (< or =3 vs > 3 years) were all significant risk factors for time to prostate-specific mortality. Using these 3 variables, tables were constructed to estimate the risk of prostate cancer-specific survival at year 15 after biochemical recurrence.
Conclusion: Clinical parameters (PSADT, pathological Gleason score, and time from surgery to biochemical recurrence) can help risk stratify patients for prostate cancer-specific mortality following biochemical recurrence after radical prostatectomy. These preliminary findings may serve as useful guides to patients and their physicians to identify patients at high risk for prostate cancer-specific mortality following biochemical recurrence after radical prostatectomy to enroll them in early aggressive treatment trials. In addition, these preliminary findings highlight that survival in low-risk patients can be quite prolonged.

Editorial Comment

How long does a patient live with a PSA recurrence after radical prostatectomy? The authors address this important issue in a rather small retrospective analysis of 379 men. Median time to biochemical progression after radical prostatectomy was 2 years. 17% of patients died within the median follow-up of 10 years.

The 10 and 15 years cause-specific survival from the time of PSA recurrence was 73% and 55%, respectively. Gleason score and PSA doubling time were predictors of death from prostate cancer.

The problem of a correct indication for surgical intervention and correct counseling of patient is again underlined by these data.

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Postoperative Radiotherapy After Radical Prostatectomy: A Randomised Controlled Trial

(EORTC trial 22911)

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Lancet. 2005; 366 (9485): 572-8; Comment in: Lancet. 2005; 366 (9485): 524-5.

Background: Local failure after prostatectomy can arise in patients with cancer extending beyond the capsule. We did a randomised controlled trial to compare radical prostatectomy followed by immediate external irradiation with prostatectomy alone for patients with positive surgical margin or pT3 prostate cancer.

Methods: After undergoing radical retropubic prostatectomy, 503 patients were randomly assigned to a wait-and-see policy, and 502 to immediate postoperative radiotherapy (60 Gy conventional irradiation delivered over 6 weeks). Eligible patients had pN0M0 tumours and one or more pathological risk factors: capsule perforation, positive surgical margins, invasion of seminal vesicles. Our revised primary endpoint was biochemical progression-free survival. Analysis was by intention to treat.

Findings: The median age was 65 years (IQR 61-69). After a median follow-up of 5 years, biochemical progression-free survival was significantly improved in the irradiated group (74.0%, 98% CI 68.7-79.3 vs 52.6%, 46.6-58.5; $p < 0.0001$). Clinical progression-free survival was also significantly improved ($p = 0.0009$). The cumulative rate of locoregional failure was significantly lower in the irradiated group ($p < 0.0001$). Grade 2 or 3 late effects were significantly more frequent in the postoperative irradiation group ($p = 0.0005$), but severe toxic toxicity (grade 3 or higher) were rare, with a 5-year rate of 2.6% in the wait-and-see group and 4.2% in the postoperative irradiation group ($p = 0.0726$).

Interpretation: Immediate external irradiation after radical prostatectomy improves biochemical progression-free survival and local control in patients with positive surgical margins or pT3 prostate cancer who are at high risk of progression. Further follow-up is needed to assess the effect on overall survival.

Editorial Comment

The problem of positive surgical margins after radical prostatectomy is common. The question is the best adjuvant treatment in this scenario, immediate or deferred radiotherapy? This important paper gives a definite answer.

Time to failure was significantly longer in the immediate radiotherapy group, with 21.4% of patients failing after 5 years in this group vs 44.2% in the deferred treatment group. Data on survival differences are not mature yet.

Immediate adjuvant radiation should be considered in margin-positive patients after radical therapy.

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