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Original research article

Postoperative radiotherapy in prostate cancer: Analysis of prognostic factors in a series of 282 patients

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ABSTRACT

Aim: To assess the outcomes of patients treated with postoperative RT in relation to the possible prognostic factors.
Background: Postoperative radiotherapy (RT) has been proved to reduce the risk of biochemical recurrence in high-risk prostate cancer patients. Baseline prostate specific antigen (PSA), pathological Gleason score (GS), positive surgical margins, nodal status and seminal vesicle invasion are independent predictors of biochemical relapse.
Materials and methods: The clinical records of 282 patients who underwent postoperative RT were retrospectively reviewed. The prognostic value of postoperative PSA, preoperative risk class, nodal status, pathological GS, margins status, and administration of hormonal therapy (HT) was analyzed.
Results: Postoperative RT was delivered with a median dose to the prostatic fossa of 66 Gy (range 50–72) in 1.8–2 Gy/fraction. Median follow-up was 23.1 months (range 6–119). Five-year actuarial biochemical disease-free survival (bDFS) and overall survival rates were 76% and 95%, respectively. Higher bDFS was found for patients with postoperative PSA <0.02 ng/ml ($p = 0.03$), low preoperative risk class ($p = 0.01$), pN0 ($p = 0.003$), GS 4–6 ($p = 0.0006$), no androgen deprivation therapy ($p = 0.02$), and irrespective of surgical margin status ($p = 0.10$). Multivariate analysis showed that postoperative PSA and Gleason score had a significant impact on bDFS ($p = 0.039$ and $p = 0.05$, respectively).

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Conclusions: Postoperative RT with a dose of 66 Gy offers an acceptable toxicity and an optimal disease control after radical prostatectomy in patients with different risk features. A postoperative PSA >0.02 ng/ml could be considered as a prognostic factor and a tool to select patients at risk for progression.

1. Background

Radical prostatectomy (RP) and radiation therapy (RT) are both effective treatment alternatives for men with localized, low- and intermediate-risk prostate cancer (PCa).[1,2] Approximately 15–25% of patients who undergo RP for localized PCa will experience cancer recurrence, diagnosed initially as biochemical recurrence (BCR).[2,3]

For high-risk localized PCa, RP is a potentially attractive treatment option, providing definitive information about pathology and an excellent loco-regional control.[2] However, the risk of biochemical recurrence ranges from 30%[3] to 68%[4] in patients with high risk features.

Baseline prostate-specific antigen (PSA), pathological Gleason score (GS), positive surgical margins, nodal status and seminal vesicle invasion are independent predictors of biochemical relapse.[5,6]

Short post-RP PSA doubling time, high pathologic Gleason score (8–10), and short disease-free interval from RP to BCR were proven to be significant risk factors for progression to distant metastases and PCa-specific mortality.[7,8]

Recently, three large randomized controlled trials (SWOG 8794, EORTC 22911, and ARO 96-02) have demonstrated that postoperative radiotherapy reduces the risk of biochemical recurrence and improves local control in patients with adverse risk factors compared with watchful waiting.[9–11] One phase 3 trial showed a reduced risk of metastasis and increased survival.[12]

Although the benefits of postoperative RT are clear, no data from randomized trials comparing adjuvant (ART) and salvage (SRT) radiotherapy are available.

At present there is not a clear definition of "salvage" RT since the definition of "detectable" PSA is still ambiguous: modern ultrasensitive PSA assays (measuring 0.001 ng/ml) were not available when the major trials regarding postoperative RT were conducted.[13–16]

2. Aim

Aim of this study was to retrospectively analyze the outcome of 282 patients treated with surgery and postoperative RT in relation to the possible prognostic factors for biochemical disease-free survival.

3. Materials and methods

Two hundred and eighty-three patients with clinically localized prostate cancer underwent postoperative RT after RP at the Department of Radiotherapy of the University Hospital "Maggiore della Carità" in Novara, Italy from 1998 to 2008. Patients were discussed in a multidisciplinary group that included urologists, radiation oncologists, and medical oncologists. This retrospective study was approved by the local Ethical Committee following the regulations of our Institution.

All clinical records were carefully reviewed. The following data were extracted from clinical records: history and physical examination, including digital rectal examination, and routine serum laboratory studies (complete blood count and biochemistry panel, including alkaline phosphatase), pre-surgery PSA, risk class according to the D'Amico classification,[17] bone scan and computed tomography (CT) scan of the abdomen and pelvis according to the risk class, neoadjuvant hormonal therapy when given, time and type of surgery, pathological T and N stage (according to the American Joint Committee on Cancer 5th edition)[18] pathological Gleason score, margin status, post-operative PSA one month after surgery, adjuvant HT if given, and follow-up status.

Two different cut-off values were considered (>0.2 ng/ml and >0.02 ng/ml) to define BCR after RP. Patients were clinically evaluated every 6 months for the first 5 years after RT, and annually thereafter, with PSA assessment every 6 months. Duration of clinical follow-up was defined as the interval from the last day of RT to the date of the last contact with the patient.

BCR after postoperative RT was defined as two subsequent PSA increases (each of at least 0.1 ng/ml) above the lowest value after postoperative RT, according with data of the literature.[19,20] Biochemical disease-free survival (bDFS) was defined as the time from the last day of RT to the date of BCR using 2 thresholds at 0.2 ng/ml and 0.02 ng/ml. Survival was calculated from the date of surgery to the last contact with the patient. Overall survival (OS) reflected all deaths, either cancer-related or for other causes. When calculating biochemical control, patients were censored at the date of their last PSA measurement.

Acute and late toxicity was scored by using the RTOG toxicity scale.[21]

3.1. *Statistical analysis*

Statistical analysis was carried out according to different clinical aspects: preoperative risk class, margins status, pathological Gleason score, postoperative PSA and administration of concomitant/adjuvant HT.

Survival was calculated using the Kaplan–Meier method[22] and comparison between groups was performed using the log-rank test.