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## Functional Outcomes and Quality of Life After Radical Prostatectomy Only Versus a Combination of Prostatectomy with Radiation and Hormonal Therapy

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### Abstract

**Background:** While the optimal use and timing of secondary therapy after radical prostatectomy (RP) remain controversial, there are limited data on patient-reported outcomes following multimodal therapy.

**Objective:** To assess the impact of additional radiation therapy (RT) and/or androgen deprivation therapy (ADT) on urinary continence, potency, and quality of life (QoL) after RP.

**Design, setting, and participants:** Among 13 150 men who underwent RP from 1992 to 2013, 905 received RP + RT, 407 RP + ADT and 688 RP + RT + ADT.

**Outcome measurements and statistical analyses:** Urinary function, sexual function, and overall QoL were evaluated annually using self-administered validated questionnaires. Propensity score-matched and bootstrap analyses were performed, and the distributions for all functional outcomes were analyzed as a function of time after RP.

**Results and limitations:** Patients who received RP + RT had a 4% higher overall incontinence rate 3 yr after surgery, and 1% higher rate for severe incontinence (>3 pads/24 h) compared to matched RP-only patients. ADT further increased the overall and severe incontinence rates by 4% and 3%, respectively, compared to matched RP + RT patients. RP + RT was associated with an 18% lower rate of potency compared to RP alone, while RP + RT + ADT was associated with a further 17% reduction compared to RP + RT. Additional RT reduced QoL by 10% and additional ADT by a further 12% compared to RP only and RP + RT, respectively. The timing of RT after RP had no influence on continence, but adjuvant compared to salvage RT was associated with significantly lower potency (37% vs 45%), but higher QoL (60% vs 56%). Limitations of

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our study include the observational study design and potential for selection bias in the treatments received.

**Conclusions:** Secondary RT and ADT after RP have an additive negative influence on urinary function, potency, and QoL. Patients with high-risk disease should be counseled before RP on the potential net impairment of functional outcomes due to multimodal treatment.

**Patient summary:** Men with high-risk disease choosing surgery upfront should be counseled on the potential need for additional radiation and or androgen deprivation, and the potential net impairment of functional outcomes arising from multimodal treatment.

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## 1. Introduction

Recent guidelines recommend that patients with high-risk prostate cancer undergoing local therapy should be informed about multimodal therapy approaches, including radical prostatectomy (RP), radiation therapy (RT), and androgen deprivation therapy (ADT) [1]. Randomized clinical trials have been shown that adjuvant RT reduces the risk of biochemical recurrence (BCR) among men with adverse prostatectomy pathology [2–5]. However, this results in overtreatment of a proportion of men with adverse pathology features who were not destined to experience BCR. Recent studies from the USA have revealed a decline in the use of adjuvant RT over time [6]. An alternative option is early salvage RT at the time of BCR. Randomized data comparing adjuvant versus early salvage RT are not yet available. Briganti et al [7] reported 2-yr and 5-yr survival rates in a propensity-matched analysis [7].

ADT is frequently added to RT, although there is no randomized trial evaluating its oncologic effect [1]. Briganti and colleagues reported that RT plus ADT significantly improved cancer-specific survival of pT2–4 pN1 patients, regardless of the extent of nodal invasion, when compared to patients receiving ADT only [8].

Although additional RT with or without ADT may be efficacious in some patients, there are a few studies with inconsistent findings on quality of life (QoL) after RT + ADT [9–14]. Most of these studies were small with heterogeneous populations or lacked patient-reported outcomes. Longitudinal comparisons of individual patients before and after RT are also lacking, as are data on the functional implications of adding ADT to post-prostatectomy RT.

The objective of this study was to assess continence, potency, and QoL outcomes using annual questionnaires for a large cohort of men undergoing RP only or as part of a multimodal approach. We hypothesized that multimodal therapy would be associated with lower continence and potency rates and poorer QoL.

## 2. Patients and methods

### 2.1. Patient population

Overall, 17 918 consecutive patients who underwent RP at our institution between January 1992 and July 2013 were evaluated for this study. Of these, 4768 patients were excluded because of loss of follow-up ( $n = 1458$ ) or no evaluable information from the QoL questionnaires ( $n = 3310$ ). Patients were classified as RP only (RP group),

RP with radiation therapy (RP + RT), RP with both RT and ADT (RP + RT + ADT), or RP with ADT (RP + ADT). Following exclusions, 13 150 patients were available for analysis.

All surgical procedures were performed using a standard technique as previously described [15–17]. Data were collected prospectively in a database approved by the institutional review board. Overall, 1593 patients underwent secondary RT after initial RP. Radiation was given in >60 different institutions using a three-dimensional conformal approach. The median radiation dose was 66.6 Gy (interquartile range [IQR] 64.8–68.4). Secondary RT was limited to the prostatic bed in 50% of the patients, was extended to the seminal vesicles in 26%, and was extended to the lymph node regions in 24%. Adjuvant RT was defined as secondary therapy before BCR and up to 6 mo after RP. RT was characterized as salvage for prostate-specific antigen  $\geq 0.2$  ng/ml or if RT initiation was at least 6 mo after surgery. The median time from surgery was 3.3 mo to adjuvant RT and 16.4 mo to salvage RT. All radiation treatments were delivered using conventional fractionation (1.8 or 2.0 Gy per fraction). Of the patients who received RT, 688 (43%) underwent adjuvant or salvage ADT. An additional 407 patients received ADT without RT at a median of 12 mo (IQR 4–45) after surgery.

Urinary function was assessed as the number of pads used per 24 h stratified as follows: 0 pads; 1 safety liner; 1–2 pads; 3–5 pads; and >5 pads. For this analysis, 3–5 pads and >5 pads were grouped as  $\geq 3$  pads. Patients whose response to the questionnaire before surgery was  $\geq 1$  pad/24 h (3%) were excluded from urinary function analyses. Sexual function and QoL were evaluated annually after surgery using self-administered validated questionnaires (International Index of Erectile Function [IIEF], and European Organization for Research and Treatment of Cancer [EORTC] QoL-C30). Potency was evaluated in terms of ability to achieve sexual intercourse using a scale from 1 to 5 points for IIEF question 2: “When you had erections with sexual stimulation, how often were your erections stiff enough for penetration?” Potency was defined as  $\geq 3$  points. Evaluation of potency was restricted to men with documented good preoperative erectile function (IIEF  $\geq 19$ ) who underwent unilateral or bilateral nerve-sparing RP. QoL was assessed using two questions on global health status/QoL from the QoL-C30 questionnaire with a range from 1 (very poor) to 7 (excellent). Linear transformation was then used to calculate a standardized score on the scale 0–100% using the following formula:  $(\text{raw score} - 1)/\text{range} \times 100$ . The resulting scores were grouped as 83.3–100%, 58.3–75%, and  $\leq 50\%$ .

### 2.2. Statistical analyses

To assess the impact of additional RT and/or ADT on urinary function, sexual function, and QoL, propensity score-matched analyses were performed in regression models using variables known to be predictive of urinary function (age, extent of nerve-sparing, prostate volume, year of surgery), sexual function (age, extent of nerve-sparing, IIEF score before RP, prostate volume, year of surgery), and QoL (age, extent of nerve-sparing, prostate volume, year of surgery) as covariates. On the basis of estimated propensity scores, patients were matched 1:1 via

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