



## Original article

## Effect of repeat prostate biopsies on functional outcomes after radical prostatectomy

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Received 31 March 2017; received in revised form 3 October 2017; accepted 21 November 2017

## Abstract

**Purpose:** Growing acceptance of active surveillance (AS) results in a relevant number of patients who will undergo radical prostatectomy (RP) after multiple biopsy sessions (Bx) due to cancer progression. The effect of repeat Bx on functional outcomes after RP remains controversial.

**Methods:** Overall, 11,140 patients who underwent RP from 2007 to 2015 were analyzed. Number of Bx sessions (1 vs. 2 vs.  $\geq 3$ ) before RP was examined. Association between number of Bx sessions and erectile dysfunction (ED) and urinary incontinence (UI) was assessed by univariable and multivariable logistic regressions.

**Results:** A total of 9,797 (87.9%) had 1 Bx, 937 (8.4%) had 2 Bx, and 406 (3.6%) had 3 or more Bx. Median age was 65 years (IQR: 59–69). Increasing Bx sessions were associated with advanced age at surgery (1, 2, and  $\geq 3$  Bx: 65, 65, and 67 years,  $P < 0.001$ ); 982 (45.9%), 906 (57.9%), and 597 (60.9%) patients achieved potency at 1, 2, and 3 years after RP, respectively. On adjusted analysis repeat Bx compared to initial Bx had no influence on ED at 1, 2, and 3 years. At 1, 2, and 3 years after RP, 6,107 (87.9%), 4,825 (90.9%), and 3,696 (91.6%) patients achieved continence. Number of Bx session had no influence on UI at follow up.

**Conclusion:** Our findings demonstrate that ED and UI rates are comparable among patients undergoing RP after initial and repeat Bx sessions. This is of importance when counseling AS patients. No adverse functional outcomes are expected if AS has to be discontinued and RP as curative option is contemplated. © 2017 Elsevier Inc. All rights reserved.

**Keywords:** Active surveillance; Functional outcome; Prostate cancer; Radical prostatectomy; Repeat prostate biopsy

## 1. Introduction

In the era of prostate-specific antigen screening, prostate cancer (PCa) represents the most common noncutaneous cancer of men [1]. To diagnose PCa, prostate biopsy (Bx) is still the gold standard. However initial Bx is negative [2] in a high proportion of men. Indications for a repeat Bx consist of suspicious digital rectal examination (DRE), rising and/or persistently high prostate-specific antigen-levels and initial Bx findings such as atypical small acinar proliferation or prostatic intraepithelial neoplasia [3]. These indications

have led to a relevant number of patients presenting for RP after multiple Bx.

Furthermore, screening and diagnostic practices resulted in a significant number of patients diagnosed with low-risk cancer. As an effort to lower overtreatment and PCa treatment specific morbidity such as ED or UI, there has been a rise of active surveillance (AS) as first line treatment for low-risk PCa [4]. To date, there is a lack of genetic or molecular predictive markers or imaging techniques, which are reliable enough to replace repeat Bx in AS protocols for detection of cancer progression. A relevant percentage of patients on AS with at least 2 prior Bx will require curative active treatment due to clinical progression [5]. One of these treatment options is RP.

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Multiple prostate Bx can cause local inflammation and trauma [6]. Periprostatic vasculature and nerves may be at risk considering the current recommendation of taking peripherally directed biopsy cores [6]. In fact, several authors have found a negative effect of number of Bx on erectile function [7–9] early after Bx. Prostatitis, edema and hematoma, which are common complications of Bx [10], have been discussed as complicating factors to find surgical planes [11,12]. There are different reports about repeat Bx not impairing the pathological and oncologic outcome of patients treated by RP [13–15]. But data about functional outcome is rare. It has been postulated that repeat Bx before RP worsens erectile function at 6-month follow-up (FU) [11], whereas other authors did not observe any differences in erectile or urinary function [16] at 12-month FU. Long-term data about urinary and erectile function in patients who underwent RP after repeat Bx is lacking. It is known that there are high rates of patients being initially incontinent or impotent, achieving continence and potency in the course of time [17,18].

Therefore, we hypothesized that multiple Bx sessions may be associated with worse functional outcome after RP. Our aim was to investigate a large European cohort to determine if repeat prostate Bx sessions are associated with adverse functional outcome after RP in short- and long-term FU.

## 2. Patients and methods

We analyzed 15,840 patients who underwent RP between January 2007 and April 2015 at the Martini-Klinik Prostate Cancer Center. Patients who underwent RP as a palliative treatment and with history of prior radiotherapy ( $n = 410$ ) were excluded. Patients with androgen deprivation therapy (ADT) or radiation therapy within the first 36 months after RP ( $n = 1,078$ ) and patients with preoperative ED or unknown erectile function before RP were excluded from the analysis for ED. A total of 3,212 patients had to be excluded because of incomplete data. Overall, 11,140 patients were left for final analysis. Information on 12-, 24-, and 36-month UI (ED) was available for 6,406, 4,861, and 3,677 (2,048, 1,481, and 928) patients, respectively.

Data were collected prospectively in an institutional review board-approved database in accordance with the declaration of Helsinki and is approved by the Institutional Internal Review Board. RP was performed by one of ten high-volume surgeons. RP was performed using an open retropubic approach or a robotic-assisted laparoscopic approach as previously described [19]. Pathological outcome was assessed using the American Joint Cancer Committee 2002 staging system and tumor grading was classified by the Gleason Grading system [20,21].

Patients follow-up after RP included standardized self-administered questionnaires. Questionnaires were routinely sent to all patients at 1, 2, and 3 year after RP.

Patients were stratified by number of Bx sessions prior RP, which was examined as categorical (1, 2, and  $\geq 3$ ) variable. UI was defined as use of  $> 1$  pad per day, ED as an International Index of Erectile Function-5 score  $< 19$ .

Uni- and multivariable logistic regressions were used to identify the influence of repeat Bx on functional outcome and to identify prognostic factors for ED and UI. All statistical analyses were performed using RStudio® (version 0.99.467) an integrated development environment for R (version 3.2.2) [22]. Statistical significance was defined as  $P < 0.05$ .

## 3. Results

### 3.1. Preoperative and perioperative characteristics

Of 11,140 men 9,797 (87.9%) had only 1 Bx, 937 (8.4%) had 2 Bx and 406 (3.6%) had 3 or more Bx sessions. Demographic characteristics stratified by number of Bx sessions are displayed in Table 1. Median age at RP was 65 years (IQR: 59–69). More Bx sessions were associated with higher age at surgery (one, two and three or more Bx sessions: 65, 65 and 67 years,  $P < 0.001$ ). Median BMI was 26.1 (IQR: 24.3–28.4). Median prostate volume was 39 ml (IQR: 30–51). Prostate volume was significantly higher in patients with more Bx sessions (38, 42 and 45 ml,  $P < 0.001$ ). Pathological outcome was more favorable in patients with repeat Bx (Supplementary data, Table 5).

RP was performed by an open retropubic approach in 9,115 patients (81.8%); a robotic-assisted laparoscopic approach (RALP) was performed in 2,025 patients (18.2%). RALP was performed significantly more often in patients with multiple Bx (17.4%, 25.1% and 21.4%,  $P < 0.001$ ). In patients with more Bx sessions, bilateral nerve-sparing was significantly more likely (69.6%, 75.7% and 79.3%;  $P < 0.001$ ).

### 3.2. Erectile dysfunction

Median International Index of Erectile Function-5 score preoperatively was 21 (IQR: 10–24) and did not differ among groups (Table 1). Overall, 1,876 patients (16.8%) used erection aids after RP. There were no differences among groups ( $P = 0.47$ ) (Table 1).

Totally, 982 (45.9%), 906 (57.9%), and 597 (60.9%) patients achieved potency at 1, 2, and 3 years after surgery, respectively. Results stratified by number of Bx sessions showed no statistically significant differences (Table 2). The multivariable logistic regression predicting erectile dysfunction at 1, 2, and 3 years after surgery is displayed in Table 3. Number of Bx sessions had no influence on erectile function.

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