

Objectives
Monitoring the serum level of prostate specific antigen (PSA) is indispensable for surveillance after radical therapy in order to identify the patients who might need additional treatment for recurrence. However, unnecessarily intensive PSA follow-up could increase medical expenses and the burden.

Methods
We retrospectively reviewed the clinicopathological data of 1,010 consecutive patients who underwent radical prostatectomy between 1995 and 2008. We excluded patients who received neoadjuvant/adjuvant therapy and those without a nadir PSA level <0.2 ng/mL. The remaining 779 patients were enrolled in this study. Biochemical recurrence (BCR) was defined as elevation of PSA to > 0.2 ng/mL. We focused on the BCR rate and the PSA doubling time (DT) following BCR at various times after surgery.

Results
During the mean follow-up period of 8.8 years, BCR occurred in 179 patients. The BCR rate per year was 6% in the first year after surgery, 6% between 1-2 years, 3% between 2-3 years, 3% between 3-5 years, and 2% at > 5 years postoperatively. The minimum PSA-DT after BCR was 1.6, 2.4, 3.1, 6.1, and 6.4 months, respectively. These minimum PSA-DTs were taken to indicate the optimal follow-up interval during each period after surgery to definitely detect BCR before the PSA exceeds 0.4 ng/mL.

Conclusions
The PSA-DT following BCR varied according to the timing after radical prostatectomy. Our data on minimum PSA-DTs after BCR are useful for setting the optimal follow-up schedule that is both necessary and sufficient.

Objectives

Radical prostatectomy is widely performed as the primary treatment for clinically localized prostate cancer and recurrence is most commonly diagnosed by detecting asymptomatic elevation of the serum level of prostate specific antigen (PSA). Therefore, monitoring serum PSA is essential for surveillance after radical therapy in order to identify patients who might need additional treatment for recurrence. Since early salvage therapy for recurrence achieves better results, it is important to detect elevation of PSA without delay. Meanwhile, unnecessarily intensive PSA monitoring is undesirable, considering both medical costs and the burden on physicians and patients.

The PSA doubling time (PSA-DT) is defined as the number of months it takes for the PSA level to double from a baseline value. Elevation of PSA after surgery is thought to reflect growth of the residual tumor, so the PSA-DT approximates the time required for the number of tumor cells to double. It is known that the PSA-DT remains relatively constant over time after BCR, and it can be used to estimate future PSA values.

In this study, in order to determine the optimal interval for measurement of PSA after surgery, we focused on the PSA-DT following BCR at various times after radical prostatectomy.

Establishment of the optimal follow-up schedule after radical prostatectomy

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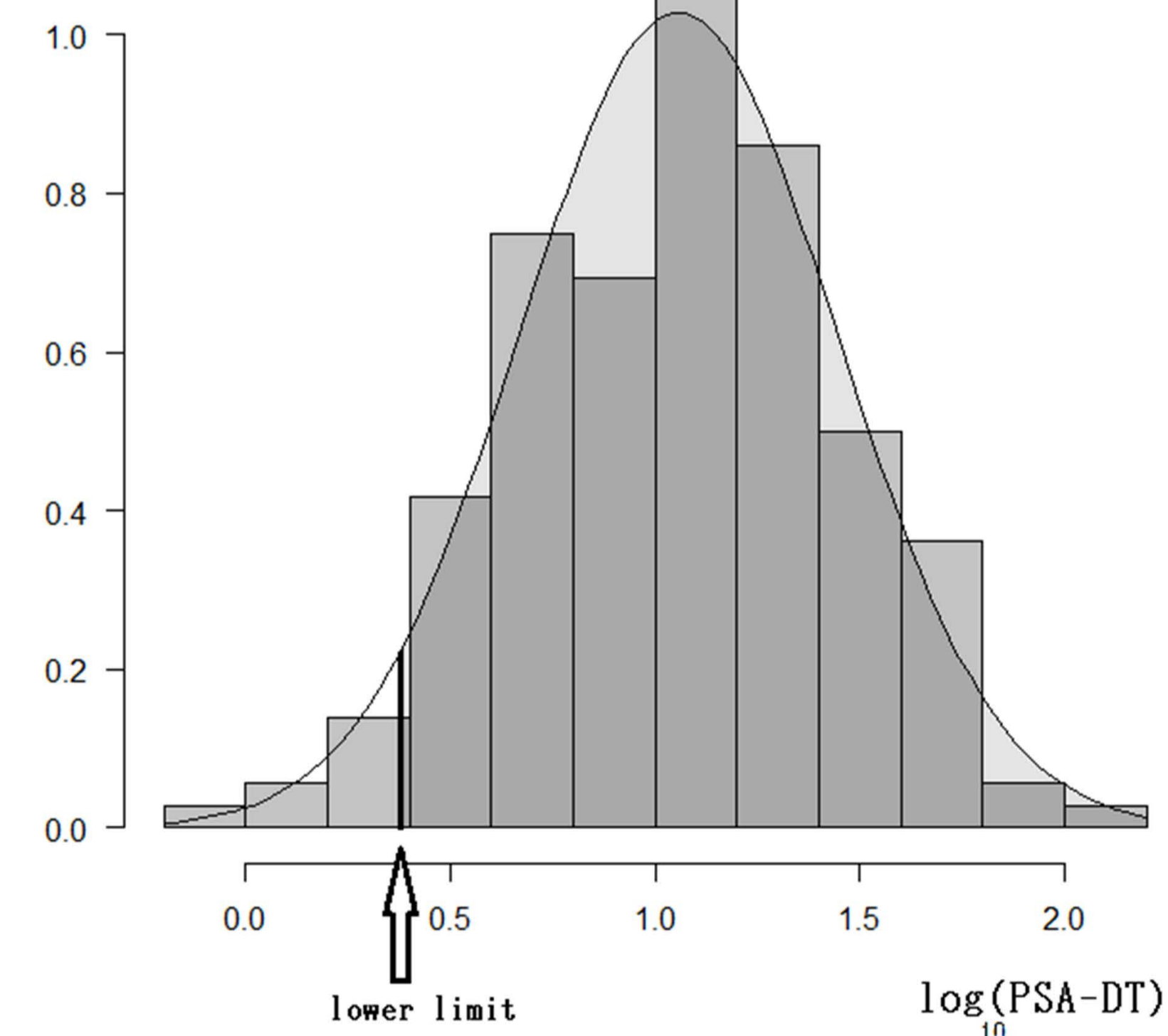
Methods

We retrospectively reviewed the clinicopathological data of 1,010 consecutive patients who underwent radical prostatectomy between 1995 and 2008. After we excluded patients who received neoadjuvant/adjuvant therapy and those without a nadir PSA level <0.2 ng/mL, the remaining 779 patients were enrolled.

Biochemical recurrence (BCR) was defined as elevation of PSA to > 0.2 ng/mL after radical prostatectomy. To detect BCR, PSA was generally measured at 3-month intervals for the first two years after surgery, at 6-months intervals for the next three years, and annually thereafter. We focused on the BCR rate and the PSA-DT following BCR at various times after radical prostatectomy. PSA-DT was calculated with a formula that employs the natural logarithm of 2 divided by the slope obtained from fitting linear regression of the natural log of PSA to time. Patients were divided into five groups by setting multiple cut points at clinically convenient times of 1, 2, 3, 5 years after surgery.

The start time of this study was the date of radical prostatectomy, and Kaplan-Meier curves were drawn to examine postoperative BCR-free survival. The PSA-DT showed a log-normal distribution, and the Shapiro-Wilk normality test gave a p value of 0.923 (Figure 1). In this study, the minimum PSA-DT was set as the one-sided lower 95% confidence limit. We considered that the ideal PSA range for detection of BCR should be set at 0.2 to 0.4 ng/mL in order to start salvage treatment before PSA exceeds 0.5 ng/mL. Therefore, the optimal (safe) follow-up interval was calculated by estimating the timing when PSA would reach 0.4 ng/mL based on the minimum (fastest) PSA-DT.

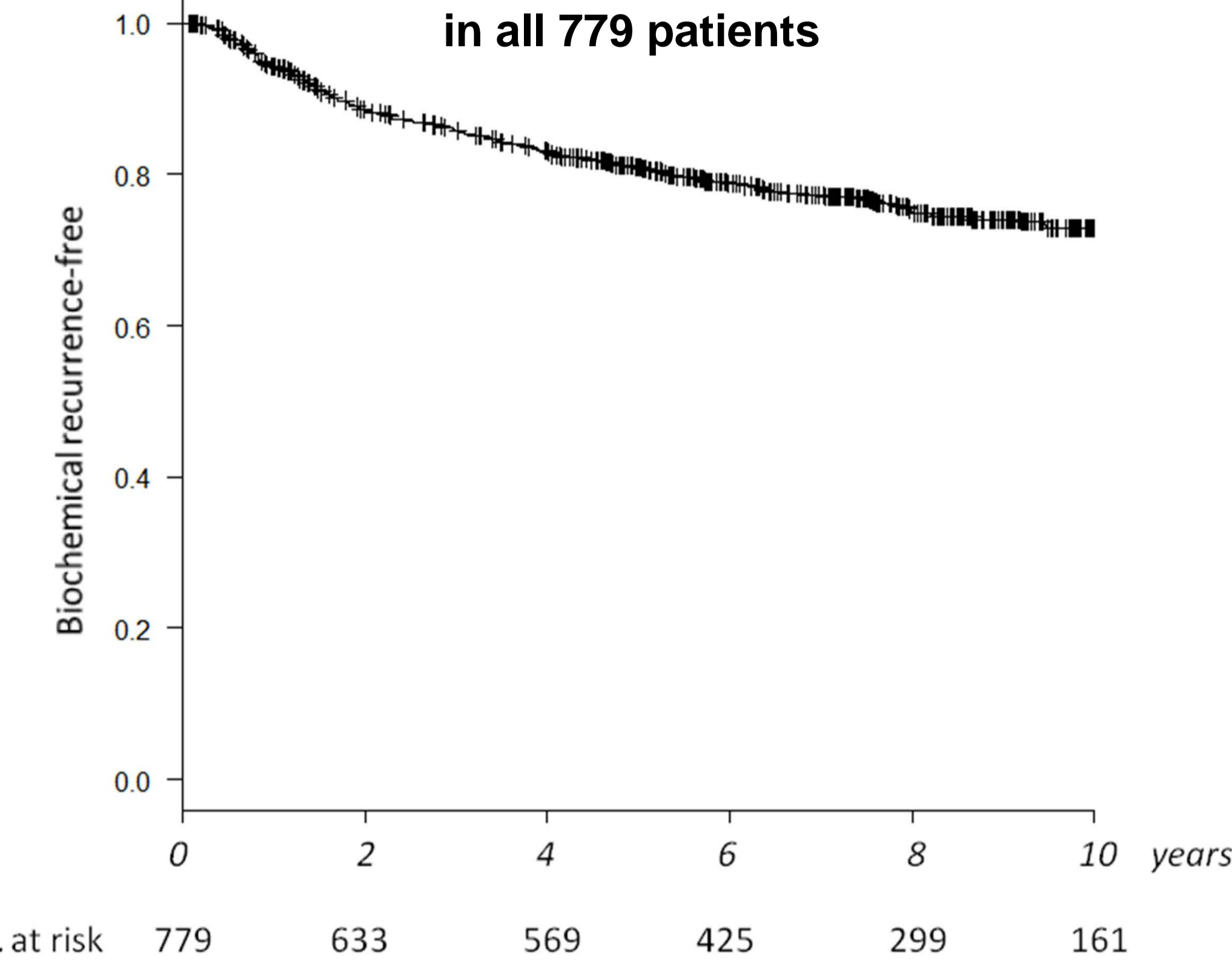
Figure 1 Histogram of the PSA-DT distribution



PSA-DT values showed a log-normal distribution. The minimum PSA-DT was defined by the one-sided lower 95% confidence limit.

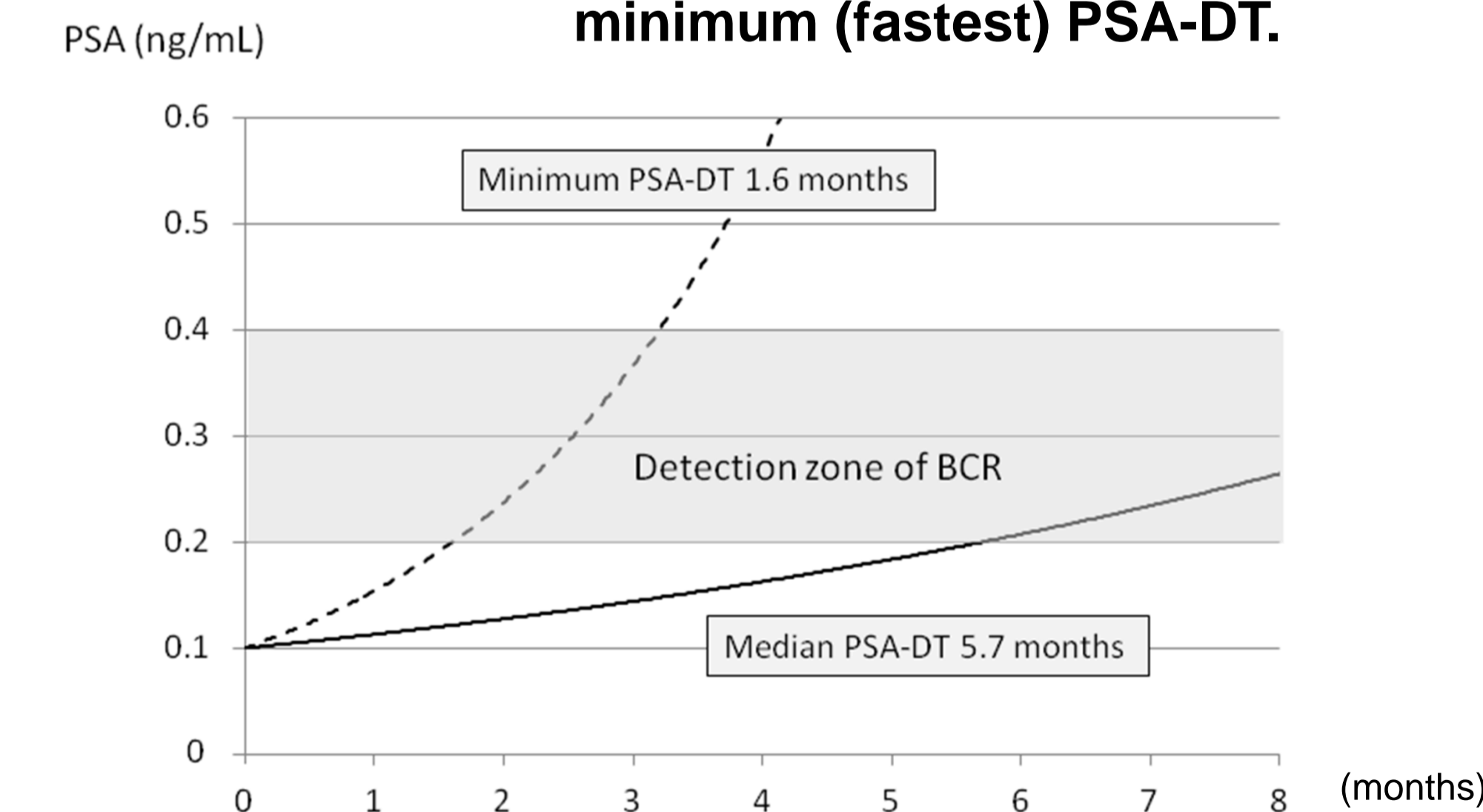
Results

Figure 2 Biochemical recurrence-free survival rates in all 779 patients



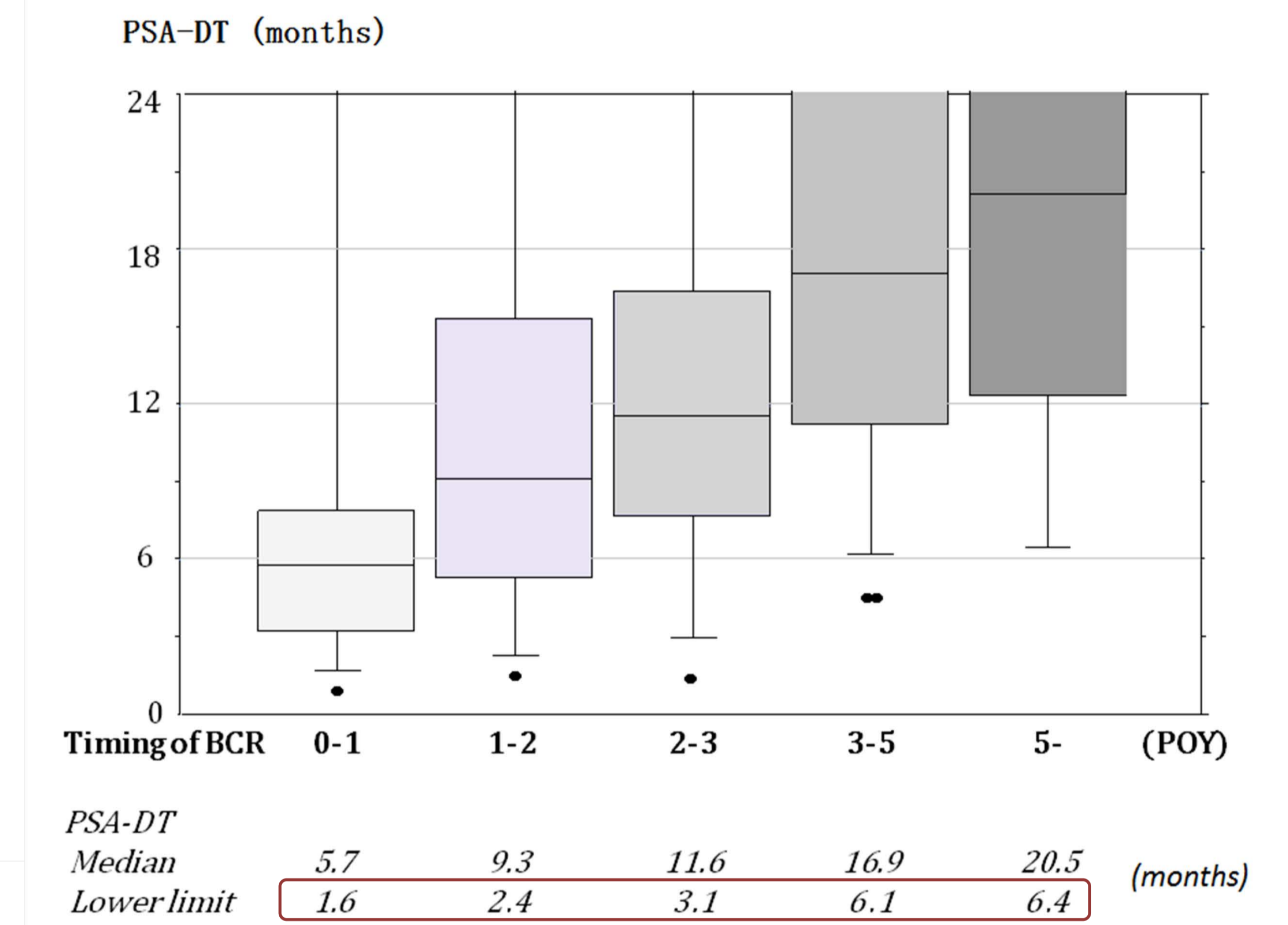
The annual BCR rate was 6% in the first year after surgery, 6% between 1-2 years, 3% between 2-3 years, 3% between 3-5 years, and 2% at > 5 years. The 2-, 5-, and 10-year BCR-free survival rates were 89%, 81%, and 73%, respectively.

Figure 4 PSA changes in patients with BCR according to the minimum (fastest) PSA-DT.



If a patient has a baseline PSA of 0.1 ng/mL and BCR occurs during the first year after surgery, PSA will exceed 0.4 ng/mL after 3.2 months with the minimum PSA-DT. In this way, the minimum PSA-DT values could be used to set the optimal follow-up interval during each period after surgery.

Figure 3 Median and minimum PSA-DT after BCR at each time after surgery.



The bottom and top of the box indicate the first and third quartiles, while the band inside the box is the median. The end of the whisker represents the lower 95% confidence limit. Dots indicate outliers.

Conclusions

Optimal follow-up interval

Timing after surgery	<1 year	1-2 years	2-3 years	>3 years
PSA value (ng/mL)				
-0.02	annually	annually	annually	annually
0.03-0.05	6-month	8-month	annually	annually
0.06-0.10	3-month	4-month	6-month	annually
0.11-0.20	1or 2-month	2-month	3-month	6-month