Usefulness of ultra-sensitive prostate-specific antigen following radical prostatectomy

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Abstract. This study aimed to evaluate the usefulness of ultra-sensitive prostate-specific antigen (PSA) following radical prostatectomy (RP). Between September, 2003 and March, 2009, a total of 311 prostate cancer patients underwent antegrade RP; following the exclusion of 111 patients due to prior hormonal therapy, 200 patients were finally included in this study. The results of the multivariate analysis identified RP Gleason score, extraprostatic extension, lymph node metastasis and PSA nadir as significant predictors of biochemical failure (P=0.0116, 0.0216, 0.0178 and <0.0001, respectively) and PSA nadir <0.008 ng/ml exhibited the highest hazard ratio (HR) [HR=26.34; 95% confidence interval (CI): 7.34-104.69]. After a median follow-up period of 52.2 months, the biochemical failure-free rate in the PSA nadir <0.008 and ≥0.008 ng/ml groups was 94.3 and 58.8%, respectively, with a statistically significant difference according to the log-rank test (P<0.001). In the multivariate analysis, statistically significant differences were observed only in pathological nodel stage within the PSA nadir <0.008 ng/ml group (P=0.0107). For this reason, post-operative follow-up using ultra-sensitive PSA is considered to be of value, since the use of high-sensitivity PSA to confirm a reduction to below postoperative measurement threshold value (PSA nadir <0.008 ng/ml) may avert administering unnecessary additional treatment, regardless of pathological reccurrence factors.

Introduction

Prostate-specific antigen (PSA) has long been proven to be effective as a tumor marker in prostate cancer cases (1). In particular, PSA is most effective when used as a post-treatment monitor. In cases of radical prostatectomy (RP), the mere detection of PSA postoperatively is highly likely to signify residual lesions (2). In addition, postoperative follow-up of prostate cancer cases is currently implemented mainly by using PSA and rectal examination. Our institution also uses PSA in the follow-up of postoperative RP cases and, from September, 2003 onwards, has been using ultra-sensitive PSA (ARCHITECT®automated immunoassay analyser, Abbott Laboratories; measurement threshold 0.008 ng/ml). Ultra-sensitive PSA enables earlier detection of PSA recurrence compared to that with conventional reagents (3-5). However, the effectiveness of additional treatment in regard to PSA recurrence postoperatively in RP cases remains debatable (6,7) and unnecessary treatment should generally be avoided. It is hypothesized that urologists may have experience with cases in which, since PSA does not simply continue to increase postoperatively, decision making as to the timing of additional treatment may be challenging, even when pathological factors for recurrence are taken into consideration. For this reason, we investigated the effectiveness of ultra-sensitive PSA and its value in averting the administration of additional treatment, using transitions in ultra-sensitive PSA in patients who have undergone RP.

Materials and methods

Patient characteristics. A total of 311 patients underwent prostate biopsy and were diagnosed with prostate cancer at the National Kyushu Cancer Center (Fukuoka, Japan) and additional associated institutions. Tissue specimens, obtained from the 311 patients between September, 2003 and March, 2009 were reviewed in embedded whole-mount antegrade RP specimens with adenocarcinoma. All the patients underwent pelvic lymph node dissection during the same time period. A total of 111 patients were excluded from this study due to prior hormonal therapy. The profile of the patients is summarized in Table I. All the patients were Japanese and the median follow-up after surgery was 52.2 months. The median age of the patients was 66 years (range, 47-77 years) and the preoperative PSA was 7.704 ng/ml (range, 0.959-39.413 ng/ml). The number of cases with clinical ≥T2 and pathological ≥T3 disease was 102 (51.0%) and 64 (32.0%), respectively. The number of patients with an RP Gleason score of ≥8 was 44

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Key words: prostate cancer, ultra-sensitive prostate-specific antigen, prostate-specific antigen nadir, biochemical failure, radical prostatectomy, Japanese

Table I. Patient clinicopathological profile.

Characteristics	Total, no. (%) (n=200)	BCF (-), no. (%) [n=183 (91.5)]	BCF (+), no. (%) [n=17 (8.5)]
Median age, years (range)	66 (47-77)	66 (47-77)	70 (57-75)
Median preoperative PSA, ng/ml (range)	7.704 (0.959-39.413)	7.590 (0.959-39.413)	8.115 (5.024-25.577)
Clinical stage, n (%)			
cT1c	98 (49.0)	94 (51.4)	4 (23.5)
≥cT2	102 (51.0)	89 (48.6)	13 (76.5)
Pathological stage, n (%)			
≤pT2	136 (68.0)	130 (71.0)	6 (35.3)
≥pT3	64 (32.0)	53 (29.0)	11 (64.7)
RP Gleason score, n (%)			
≤7	156 (78.0)	147 (80.3)	9 (52.9)
≥8	44 (22.0)	36 (19.7)	8 (47.1)
EPE, n (%)			
0	140 (70.0)	134 (73.2)	6 (35.3)
1	60 (30.0)	49 (26.8)	11 (64.7)
RM, n (%)			
0	168 (84.0)	156 (85.2)	12 (70.6)
1	32 (16.0)	27 (14.8)	5 (29.4)
pN, n (%)			
0	197 (98.5)	182 (99.5)	15 (88.2)
1	3 (1.5)	1 (0.5)	2 (11.8)
PSA nadir, ng/ml [n (%)]			
<0.008	183 (91.5)	173 (94.5)	10 (58.8)
≥0.008	17 (8.5)	10 (5.5)	7 (41.2)

BCF, biochemical failure: two consecutive values ≥0.2 ng/ml; PSA, prostate-specific antigen; RP, radical prostatectomy; EPE, extraprostatic extension; RM, resection margin.

(22.0%). The number of patients with extraprostatic extension (EPE), positive resection margin and positive lymph nodes was 60 (30.0%), 32 (16.0%) and 3 (1.5%), respectively.

PSA nadir and biochemical failure. The PSA nadir was defined as the lowest PSA value following RP and the measurement limit of serum PSA values was <0.008 ng/ml in this study. In 183 patients (91.5%), the serum PSA levels were decreased to <0.008 ng/ml. Biochemical failure following RP was defined as two consecutive PSA values of ≥0.2 ng/ml (8).

Follow-up. The follow-up schedule following RP involved a PSA assay every 3 months for the first 2 years, every 4 months for the following 3 years and every 6 months thereafter. A pathologist evaluated the degree of malignancy of the prostatectomy specimens, according to the 2005 International Society of Urological Pathology Consensus Conference on Gleason grading system (9), and the pathological stage, based on the 2009 TNM classification (10).

Statistical analysis. Univariate and multivariate analyses were also performed using the Cox proportional hazards regression model, in order to identify the predictors associated with biochemical failure following RP. The variables were as follows: age, preoperative PSA, clinical T stage, pathological T stage, RP Gleason score, EPE, resection margin status, lymph node metastasis and PSA nadir. The biochemical failure-free rate was determined using the Kaplan-Meier method. The log-rank test was used to determine the differences among the cases in the PSA nadir group. The Kruskal-Wallis test was used to determine the differences among the cases in the PSA transition type group. The statistical analyses were performed using the JMP® version 8 software program (SAS Institute, Inc., Cary, NC, USA). P<0.05 was considered to indicate a statistically significant difference.

Results

Correlation between clinicopathological characteristics and biochemical failure. The correlation between the clinicopathological characteristics and biochemical failure is presented in Table II. According to the Cox proportional hazards analysis, preoperative characteristics, such as age and clinical tumor stage, were significant predictors. Postoperative characteristics, such as pathological tumor stage, RP Gleason score, EPE, lymph node metastasis and PSA nadir were found

Table II. Correlation between clinicopathological characteristics and biochemical failure.

Characteristics	Hazard ratio	P-value	95% CI
Univariate analysis			
Age	1.0954	0.0401	1.0039-1.2111
Preoperative PSA	1.0608	0.1041	0.9859-1.1196
cT1 vs. ≥cT2	3.5756	0.0157	1.2567-12.7632
pT2 vs. pT3	4.1182	0.0041	1.5666-11.9563
RP Gleason score ≤7 vs. ≥8	3.1470	0.0235	1.1760-8.2754
EPE0 vs. EPE1	4.4515	0.0025	1.6934-12.9237
RM0 vs. RM1	2.5284	0.1064	0.8023-6.8439
pN0 vs. pN1	14.4627	0.0097	2.2538-52.7430
PSA nadir (<0.008 vs. ≥0.008 ng/ml)	11.7402	<0.0001	4.2154-30.9738
Multivariate analysis			
RP Gleason score ≤7 vs. ≥8	5.2407	0.0116	1.4613-19.6442
EPE0 vs. EPE1	3.1760	0.0216	1.1835-9.4170
pN0 vs. pN1	11.9323	0.0178	1.6884-55.7366
PSA nadir (<0.008 vs. ≥0.008 ng/ml)	26.3362	<0.0001	7.3445-104.6937

CI, confidence interval; PSA, prostate-specific antigen; RP, radical prostatectomy; EPE, extraprostatic extension; RM, resection margin.

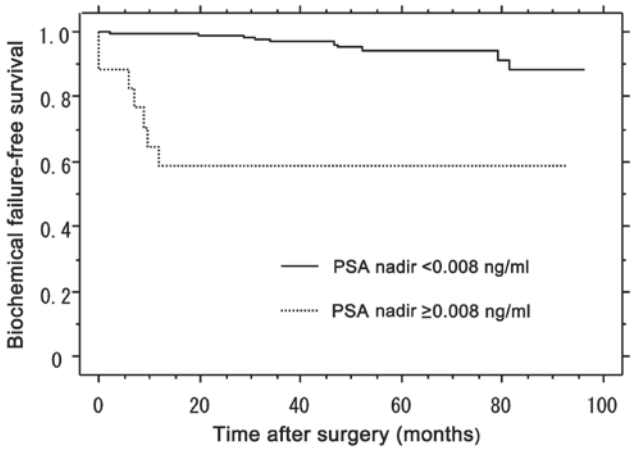

Figure 1. Biochemical failure-free survival of patients stratified by the prostate-specific antigen (PSA) nadir value (<0.008 vs. ≥0.008 ng/ml).

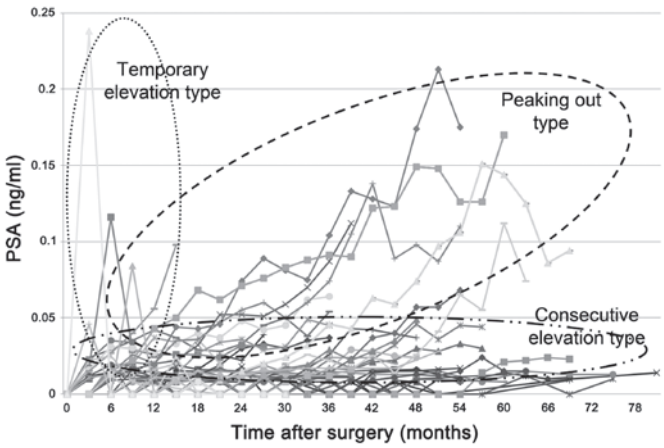

Figure 2. Prostate-specific antigen (PSA) transition with PSA ≥0.008 ng/ml after a PSA nadir of <0.008 ng/ml.

to be significant predictors based on the univariate analysis, whereas according to the multivariate analysis, statistically significant differences were found in the RP Gleason score, EPE, lymph node metastasis and PSA nadir <0.008 ng/ml (P=0.0116, 0.0216, 0.0178 and <0.0001, respectively). PSA nadir <0.008 ng/ml exhibited the highest hazard ratio (HR) [HR=26.34, 95% confidence interval (CI): 7.34-104.69].

Biochemical failure-free survival of patients stratified by PSA nadir value (<0.008 vs. ≥0.008 ng/ml). After a median follow-up period of 52.2 months, the biochemical failure-free rate in the PSA nadir <0.008 and ≥0.008 ng/ml groups was 94.3 and 58.8%, respectively (Fig. 1). The difference between the PSA nadir <0.008 and ≥0.008 ng/ml groups was statistically significant, according to the log-rank test (P<0.001; df=2).

Clinicopathological characteristics according to biochemical failure group classificaction in the PSA nadir <0.008 ng/ml group. The profile of the patients analyzed in the PSA nadir <0.008 ng/ml group is presented in Table III. In the biochemical failure-negative group, the number of cases with clinical ≥T2 and pathological ≥T3 disease was 86 (49.7%) and 48 (27.7%), respectively. The number of patients with a Gleason score of ≥8 were 36 (20.8%). The number of patients with EPE, positive resection margin and positive lymph nodes was 44 (25.4%), 23 (13.3%) and 1 (0.6%), respectively. The number of patients with PSA ≥0.008 ng/ml after a PSA nadir of <0.008 ng/ml was 64 (35.0%).

Correlation between clinicopathological characteristics and biochemical failure in the PSA nadir <0.008 ng/ml group. The

Table III. Clinicopathological characteristics according to BCF group classificaction in the PSA nadir <0.008 ng/ml group.

Characteristics	Total, no. (%) (n=183)	BCF (-), no. (%) [n=173 (94.5)]	BCF (+), no. (%) [n=10 (5.5)]
Median age, years (range)	66 (47-77)	66 (47-77)	70 (63-73)
Median preoperative PSA, ng/ml (range)	7.491 (0.959-39.413)	7.491 (0.959-39.413)	7.652 (5.024-15.403)
Clinical stage, n (%)			
cT1c	90 (49.2)	87 (50.3)	3 (30.0)
≥cT2	93 (50.8)	86 (49.7)	7 (70.0)
Pathological stage, n (%)			
≤pT2	129 (70.5)	125 (72.3)	4 (40.0)
≥pT3	54 (29.5)	48 (27.7)	6 (60.0)
RP Gleason score, n (%)			
≤7	141 (77.0)	137 (79.2)	4 (40.0)
≥8	42 (33.0)	36 (20.8)	6 (60.0)
EPE, n (%)			
0	133 (72.7)	129 (74.6)	4 (40.0)
1	50 (27.3)	44 (25.4)	6 (60.0)
RM, n (%)			
0	158 (86.3)	150 (86.7)	8 (80.0)
1	25 (13.7)	23 (13.3)	2 (20.0)
pN, n (%)			
0	180 (98.4)	172 (99.4)	8 (80.0)
1	3 (1.6)	1 (0.6)	2 (20.0)
PSA ≥0.008 ng/ml after PSA nadir, n (%)	64 (35.0)	54 (31.2)	10 (100)

BCF, biochemical failure: two consecutive values ≥0.2 ng/ml; PSA, prostate-specific antigen; RP, radical prostatectomy; EPE, extraprostatic extension; RM, resection margin.

Table IV. Correlation between clinicopathological characteristics and biochemical failure in the PSA nadir <0.008 ng/ml group.

Characteristics	Hazard ratio	P-value	95% CI
Univariate analysis			
Age	1.1296	0.0436	1.0032-1.3040
Preoperative PSA	1.0079	0.9009	0.8635-1.1061
cT1 vs. ≥cT2	2.6392	0.1439	0.7252-12.3618
pT2 vs. pT3	3.4898	0.0506	0.9967-13.6517
RP Gleason score ≤7 vs. ≥8	5.0577	0.0127	1.4269-20.0230
EPE0 vs. EPE1	3.7401	0.0394	1.0676-14.6372
RM0 vs. RM1	1.7780	0.4933	0.2680-7.1155
pN0 vs. pN1	33.1399	0.0020	4.8130-146.0192
Multivariate analysis			
pN0 vs. pN1	17.5434	0.0107	2.1922-111.5099

PSA, prostate-specific antigen; CI, confidence interval; RP, radical prostatectomy; EPE, extraprostatic extension; RM, resection margin.

correlation between the clinicopathological characteristics and biochemical failure in the PSA nadir <0.008 ng/ml group is presented in Table IV. According to the Cox proportional hazards analysis of the PSA nadir <0.008 ng/ml group, age, RP Gleason score, EPE and lymph node metastasis were found to be significant predictors based on the univariate analysis (P=0.0436, 0.0127, 0.0394 and 0.0020, respectively). However, in the multivariate analysis, statistically significant differences were only observed in pathological nodal stage (pN) (P=0.0107).

Table V. Clinicopathological characteristics according to PSA transition types in the group with PSA≥0.008 after a PSA nadir of <0.008 ng/ml.

Characteristics	Total (n=64)	Type of transition: Temporary elevation, no. (%) [n=18 (28.1)]	Peaking out[a], no. (%) [n=33 (51.6)]	Consecutive elevation[b], no. (%) [n=13 (20.3)]	P-value
Median age, years (range)	67 (50-78)	63 (50-74)	70 (63-73)	70 (63-73)	0.3431
Median preoperative PSA, ng/ml (range)	7.951 (1.477-22.632)	6.562 (3.232-11.410)	8.116 (1.477-22.632)	7.919 (5.024-13.388)	0.6013
Pathological stage, n (%)					0.0003
≤pT2	38 (59.4)	17 (94.4)	18 (54.5)	3 (23.1)	
≥pT3	26 (40.6)	1 (5.6)	15 (45.5)	10 (76.9)	
RP Gleason score, n (%)					0.8242
≤7	45 (70.3)	12 (66.7)	23 (69.7)	10 (76.9)	
≥8	19 (29.7)	6 (33.3)	10 (30.3)	3 (23.1)	
EPE, n (%)					0.0003
0	41 (64.1)	17 (94.4)	21 (63.7)	3 (23.1)	
1	23 (35.9)	1 (5.6)	12 (36.3)	10 (76.9)	
RM, n (%)					0.1950
0	50 (78.1)	16 (88.9)	26 (78.8)	8 (61.5)	
1	14 (21.9)	2 (11.1)	7 (21.2)	5 (38.5)	

[a]0.008≤PSA<0.05. [b]PSA≥0.05. PSA, prostate-specific antigen; RP, radical prostatectomy; EPE, extraprostatic extension; RM, resection margin.

PSA transition with PSA ≥0.008 ng/ml after a PSA nadir of <0.008 ng/ml (Fig. 2). i) Temporary elevation, defined as cases demonstrating temporary PSA elevation followed by a decrease to <0.008 ng/ml, was observed in 18 cases (28.1%); ii) peaking out, defined as 0.008≤PSA<0.05 ng/ml, was observed in 33 cases (51.6%); and iii) consecutive elevation, defined as PSA ≥0.05 ng/ml, was observed in 13 cases (20.3%).

Clinicopathological characteristics according to PSA transition types in the group with PSA ≥0.008 ng/ml after a PSA nadir of <0.008 ng/ml. The profile of the patients who were analyzed in the PSA ≥0.008 ng/ml after a PSA nadir of <0.008 ng/ml group is presented in Table V. The number of cases with temporary elevation, peaking out and consecutive elevation type of transition was 18 (28.1%), 33 (51.6%) and 13 (20.3%), respectively. According to the Kruskal-Wallis test analysis, statistically significant differences were observed in pathological stage and EPE (both P=0.0003).

Discussion

Thompson *et al* (11) reported that adjuvant radiotherapy following RP for stage pT3N0M0 prostate cancer significantly reduces the risk of metastasis and increases survival (P=0.016 and 0.023, respectively). Furthermore, according to Bolla *et al* (12), the results at a median follow-up of 10.6 years indicated that conventional postoperative irradiation significantly improves biochemical progression-free survival and local control compared to a wait-and-see policy, supporting the results at 5-years of follow-up (P=0.001); however, the improvements in clinical progression-free survival were not maintained. Late adverse effects (any type of any grade) were more frequent in the postoperative irradiation compared to the wait-and-see group (P=0.001) (12). In addition, Shen *et al* (13) reported that, even in cases with a positive resection stump, there were at least a few in which PSA was decreased below the measurement threshold or in which no PSA was detected. The authors of the present study have had a similar experience, in which decision making regarding additional treatment has often been challenging, in light of clinical factors such as age and overall physical condition, even when based on pathological recurrence factors. Therefore, even in pT3 cases, it is possible that, under certain conditions, adjuvant radiotherapy may be unnecessary. If the adverse events associated with adjuvant therapy in post-RP cases are taken into consideration, it is obvious that, from the patient point of view, unnecessary treatment should be avoided.

It was previously reported that the lower the ultra-sensitive PSA nadir value postoperatively, the lower the risk of PSA recurrence (13,14). Our institution has been using ultra-sensitive PSA since September, 2003 to implement follow-up in RP cases, which, compared to the conventional methods, facilitates PSA measurement at significantly lower levels, thereby facilitating monitoring the extent of the decrease in postoperative PSA levels and the early identification of PSA recurrence. Therefore, we aimed to investigate the usefulness of ultra-sensitive PSA in Japanese prostate cancer patients and its potential value in averting unnecessary adjuvant therapy, using transitions in ultra-sensitive PSA among postoperative RP cases.

As shown in Table I, the PSA nadir was reduced to <0.008 ng/ml in 183 patients (91.5%) who had undergone RP, while biochemical failure was observed in 17 cases (8.5%). Ellis *et al* (3) reported the PSA value to be below the measurement sensitivity level of 0.008 ng/ml in 86.2% of cystoprostatectomy cases in which prostate cancer was not detected, indicating that RP is efficiently performed in this institution. In our group of cases, when factors affecting biochemical failure were considered, the RP Gleason score, EPE, lymph node metastasis and PSA nadir exhibited significant difference in the multivariate analysis (P=0.0116, 0.0216, 0.0178 and <0.0001, respectively) (Table II). Of these factors, PSA nadir <0.008 ng/ml exhibited the highest HR (HR=26.34; 95% CI: 7.34-104.69). For this reason, we next considered biochemical failure-free survival in terms of PSA nadir value in patients who underwent RP. After a median follow-up of 52.2 months, the biochemical failure-free rate in the PSA nadir <0.008 and ≥0.008 ng/ml groups was 94.3 and 58.8%, respectively (Fig. 1), with a statistically significant difference according to the log-rank test (P<0.001; df=2). From these results, we may hypothesize that the group with a PSA nadir of <0.008 ng/ml following RP was significantly less likely to experience biochemical failure compared to the group with PSA ≥0.008 ng/ml. Kinoshita *et al* (2) reported that cases where the PSA nadir value does not decrease to ≤0.01 ng/ml postoperatively using the ultra-sensitive method, are at a significant risk of PSA recurrence (>0.1 ng/ml), which is consistent with our findings. Yu *et al* (4) classed reagents with an ultra-sensitive PSA detection threshold value of 0.1-0.3 ng/ml as first-generation, those of 0.02-0.1 ng/ml as second-generation and those of 0.001-0.02 ng/ml as third-generation. The advances in these ultra-sensitive PSA reagents have enabled the selection of postoperative RP cases in which the PSA values have decreased below even the lowest measurement thresholds, indicating that unnecessary additional treatment may be avoidable, regardless of the clinical and pathological recurrence factors.

Even among patients in whom the PSA nadir value was decreased to <0.008 ng/ml, biochemical failure was observed in 10 cases (5.5%) (Table II). A possible explanation as to why these cases did not decrease to below the theoretically predicted measurement threshold following RP, i.e., did not decrease to <0.008 ng/ml using our reagents, may be that surgery was unsuccessful (residual prostate cancer tissue or presence of a small metastasis that was not detected preoperatively). Furthermore, in addition to potential problems with the reagents and measurement methods, there exists the possibility of 'noise' created by residual benign prostate tissue during measurement, or the production of PSA by the periurethral glands or other organs. Therefore, we considered the factors affecting biochemical failure only in cases in which such 'noise' had been removed as much as possible. As shown in Table II, of the 183 RP cases in which the postoperative PSA nadir value was reduced to <0.008 ng/ml, 173 cases (94.5%) did not experience biochemical failure; of note, among these cases, 48 (27.7%) were pT3. In addition, the group experiencing biochemical failure comprised 10 cases (5.5%), of which only 6 were pT3. Therefire, with pT3 used as the only criterion for determining additional treatment, in this study, 44 out of 54 cases (81.5%) would have been administered unnecessary treatment. The correlation between clinicopathological characteristics and biochemical failure in the PSA nadir <0.008 ng/ml group is shown in Table IV. In the multivariate analysis, statistically significant differences were only observed in pN (P=0.0107). In this study, however, the pN frequency was low, occurring in only 1.5% of the cases and not all such cases developed recurrence. Conventionally, metastasis to the lymph nodes is considered to reflect a poor prognosis and the addition of whole-body endocrine therapy following RP is considered the treatment of choice. Bader *et al* (15), however, reported a 78% cause-specific survival rate in patients treated with RP and extended pelvic lymph node dissection and who did not undergo any adjuvant therapy until disease progression. Of note, among those patients with 1 positive lymph node, 39% remained free of clinical or biochemical progression, compared to 12% of patients with ≥2 positive nodes.

As a result, it is currently fairly standard for transitions in postoperative PSA values to be monitored and in several cases the need for additional treatment is determined based on PSA transitions, regardless of clinical or pathological factors.

Therefore, we considered the possibility of avoiding additional treatment based on PSA transitions using ultra-sensitive PSA. A total of 64 cases (35.0%) among those with a PSA nadir value of <0.008 ng/ml increased to ≥0.008 ng/ml at least once. The transitions in ultra-sensitive PSA among all cases are shown in Table V. It was determined that there are three trends in ultra-sensitive PSA and, as a result, the cases were divided into three groups as follows: the temporary elevation type group, in which PSA levels increased temporarily, followed by a subsequent decrease to <0.008 ng/ml. According to Shimizu *et al* (16), determining PSA recurrence based on a definition of the number of consecutive times ultra-sensitive PSA increases may be challenging. The remaining cases were divided into two further groups based on the tendency for PSA to rise consecutively to a boundary of PSA 0.05 ng/ml: the consecutive elevation type group (PSA≥0.05 ng/ml) and the peaking out type group (0.008≤PSA<0.05 ng/ml). The consecutive elevation type group, which is closest to our perception of reccurrence, comprised only 20.3% of the entire group, with 51.6% of the cases falling into the peaking out category. With a single exception, the consecutive elevation type group transited to <0.05 ng/ml. As shown in Table V, when the three groups were compared, statistically significant differences were found in pathological stage (≥pT3) and EPE (both P=0.0003). Therefore, we may hypothesize that cases with the pathological factors ≥pT3 and EPE are mainly following the transition of the consecutive elevation type group. However, while only one case of each pT3 and EPE (5.6%) was found in the transient group, there were 15 cases of pT3 (45.5%) and 12 cases of EPE (36.3%) in the peaking out type group. Therefore, unnecessary additional treatment may be avoided if PSA transition patterns are taken into consideration alongside pathological recurrence factors in the peaking out type group, as ongoing observation, rather than treatment, is implemented until PSA levels are at least 0.05 ng/ml. Terai *et al* (17) reported that the lower a patient's PSA prior to curative radiotherapy, the better the response. In that study, 92% of the patients underwent curative radiotherapy at PSA levels ≤0.5 ng/ml. As a result, it may be safe to hypothesize that it is not to the patients' disadvantage to hold off additional treatment until the PSA levels rise to 0.05 ng/ml, the level the authors consider appropriate, rather

than implementing treatment immediately after surgery. Since the consecutive elevation type group, which is considered to require additional treatment, is relatively small, the use of ultra-sensitive PSA to detect transition facilitates the selection of cases that do not belong to the continuous elevation type, thereby facilitating the avoidance of unnecessary additional treatment.

The European Association of Urology guidelines state that patients with a PSA level of 0.1-0.2 ng/ml following RP do not exhibit either clinical or biochemical disease progression. Therefore, the use of an ultra-sensitive PSA assay may not justified for routine follow-up following RP (8). However, in this study, the observation of PSA transition using ultra-sensitive PSA following RP exhibited potential in enabling the selection of cases in which additional treatment may be avoided, even where pathological recurrence factors are present and, as such, is considered to be useful.

We retrospectively assessed the usefulness of ultra-sensitive PSA following RP in Japanese prostate cancer patients. The biochemical failure-free survival in RP cases with PSA nadir <0.008 ng/ml was found to be significantly lower comapred to those with PSA nadir ≥0.008 ng/ml and using ultra-sensitive PSA to confirm that postoperative values have decreased to below the measurement threshold may avert administering unnecessary additional treatment. Furthermore, in cases in which PSA levels were reduced to below the measurement threshold but increased subsequently, maintaining observation without treatment until the levels reach at least 0.05 ng/ml may also enable avoiding unnecessary additional treatment.

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