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Long-term outcomes of nonpalpable prostate cancer (T1c) patients treated with radical prostatectomy

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ABSTRACT

Purpose: Various strategies have been used to treat patients with nonpalpable prostate cancer (T1c). As one of the treatments for this stage, a radical prostatectomy was performed and the outcomes were evaluated.
Methods: Between 1993 and 2002, 117 patients with T1c received a radical prostatectomy and their follow-up were examined by the end of 2013. Patients were classified according to risk groups using prostate-specific antigen (PSA) and Gleasson score, and outcomes of respective groups were compared.
Results: Approximately 60% of patients were in low risk group, and the remaining patients were grouped into the intermediate or high risks in half. In 22% insignificant cancer was detected. Biochemical failure occurred in 14%. One patient exhibited bone metastasis, but no deaths from prostate cancer ware observed. The five and ten year overall survival rates were 92% and 75%, respectively, and the biochemical failure-free survival rates were 92% and 89%, respectively. No different outcomes were observed for the different risk groups in the overall and biochemical failure-free survival rates. T1c tumors contain a certain range of various stages of tumors, but most patients experienced favorable outcomes.
Conclusion: Radical prostatectomy as monotherapy is one of the treatment option for T1c prostate cancer patients, who have a long life span and belong to intermediate or high risk groups.

1. Introduction

Prostate cancer is a serious disease in elderly males in Japan. 51,534 individuals were diagnosed with prostate cancer in 2008, whereas 11,143 individuals died from prostate cancer in 2012.[1] These rates have been increasing significantly, which is due in part to longer life spans and changes in nutrition and circumstances. Screening for prostate cancer in aged males is more widespread, which has increased the detection of early stage prostate cancer. Nonpalpable prostate cancer (T1c) accounts for a considerable proportion of these cancers. T1c is managed using a variety of treatment strategies, including surgical removal, radiation, androgen deprivation and active surveillance. To evaluate the effectiveness of radical prostatectomy for T1c patients, the present study was undertaken with long-term follow up after radical prostatectomy.

2. Materials and methods

Between 1993 and 2002, 134 cases of T1c cancer underwent radical prostatectomy after consenting to treatment. Most patients underwent further examination after screening. These cases were confirmed as N0M0 by whole body bone scan and computed tomography of the pelvic area. A complete record of the patient outcome was obtained for 117 of these cases by the end of 2013. The present study evaluates these patients.

Prostate biopsy with 8–12 cores was performed via the perineal route. Histological classification was performed according to the original Gleason classification system.[2] Radical retropubic prostatectomy was performed with removal of the pelvic lymph nodes. In the few cases with high risk cancer, adjuvant androgen deprivation therapy was additionally performed. The prostate-specific antigen (PSA [total PSA]) level was assayed using an Architect PSA kit

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(Abbott, Chiba, Japan). After surgery, the PSA level was assayed every 3–6 months, and then every six months. Biochemical failure was defined as an increase of ≥0.2 ng/ml of PSA.

The risk of patients in stage T1c was separated according to the PSA value and Gleason classification which were based on the NCCN Guideline version 4. The cancer was staged according to the TNM (2002) Guideline.

Survival was calculated with the Kaplan–Meier method, and differences among groups were assessed by the Log–Rank test. Statistical differences were determined by the unpaired two-group t-test and p-value of ≤0.05 was considered statistical significant. All calculations were performed with SPSS statistical computer program (IBM-SPSS Inc, Tokyo, Japan) and KaleidaGraph (Hulinks, Tokyo, Japan).

3. Results

Approximately 60 of patients with T1c, whose PSA levels were ≤10 ng/ml and Gleason scores were ≤6, were in the low risk group. The remaining patients were separated into the intermediate or high risk groups in half (Tables 1 and 2). Insignificant cancer, which referred to ≤6 ng/ml of PSA and a tumor volume ≤0.5 cm^3, was observed in 22% of the tumors.

Formerly tumor invasion into the prostatic capsule was suspicious to be the presence of tumor cells beyond capsule, and classified in pT3. According to the TNM classification scheme (2002), capsular invasion was defined as pT2. Almost all tumors in specimens of pT3 patients in Table 2 placed touch or invasion into capsule, Therefore, Group of pT3 was changed to pT2, tumors of which located on capsule-line.

Biochemical failure occurred in 14% of all patients. Durations between diagnosis and biochemical failure were 52 ± 40 months. One patient in the high risk group experienced clinical failure and was treated with combined androgen deprivation therapy (LHRH plus bicalutamide). There was no relationship between the risk groups and pathological tumor stages (Table 2). There were no prostate cancer-specific deaths (Table 3).

The overall and biochemical failure-free survival rates are shown in Figs. 1 and 2, respectively. The overall survival rates were 92% and 75%, whereas the biochemical failure-free survival rates were 92 and 89% at five and ten years after surgery, respectively. The average age of the patients was 68 ± 5.8 years at the time of operation. According to the statistics of the Ministry of Health, Labor and welfare Japan (2000), the average life term is 18.8 years (65 years old) and 15.1 years (70 years old), therefore, surgery does not seem to have an effect on life span. There were no significant differences in the overall and biochemical failure-free survival rates of the different risk groups (Figs. 3 and 4). Despite the wide range of the pathological extent associated with T1c, the postoperative courses proceeded in a similar and favorable manner.

Table 1
Patient characteristics.

		No. cases
Age	≤60 yrs	14 (12)
	61–70	66 (56)
	≥71	37 (32)
PSA	≤10 ng/ml	73 (62)
	11–20	27 (23)
	≥21	15 (13)
	Unknown	2 (2)
Gleason score	≤6	62 (53)
	7	28 (24)
	≥8	16 (14)
	Unknown	11 (9)

Number in parenthesis is the ratio to respective item.

Table 2
Relationship between risk and pathological findings.

Risk	pT2ab	pT2c	pT3	Total no. cases
Low	31 (45)	28 (38)	12 (17)	69
Intermediate	11 (44)	10 (40)	4 (16)	25
High	11 (48)	10 (43)	2 (9)	23

Invasion to the capsule is staged as pT3.
Number in parenthesis is the ratio to each risk group.

Table 3
Outcome of patients.

	No. cases
Biochemical failure	16[a] (14)
Clinical failure (bone)	1 (0.9)
Cause-specific death	0
Death of other causes	34 (29)
Malignancy	11
Pneumonia	6
Cerebral apoplexy	4
Cardiac disease	4
Others	9

Number in parenthesis is the ratio to whole patients (117 cases).
[a] Includes clinical failure case.

4. Discussion

Nonpalpable prostate cancer, designated as T1c, includes a wide range of stages.[3] Operative specimens of T1c from the Johns Hopkins Hospital revealed the following tumors: 16% of insignificant cancer, 10% of minimal extent cancer (organ-confined, 0.2–0.5 cm^3 of volume and <7 ng/ml of PSA), 37% of moderately extent cancer (penetrated, >0.5 cm^3 and >7 ng/ml of PSA) and 37% of advanced cancer.[4] Continuing to this report, the proportion of insignificant cancer in operated T1c specimens exhibited 30.7%, whereas 19.6% was advanced cancer.[5] In other Institutes, the proportion of insignificant cancer in operated T1c specimens has been reported to account for approximately 20–40 % of cases, including the present

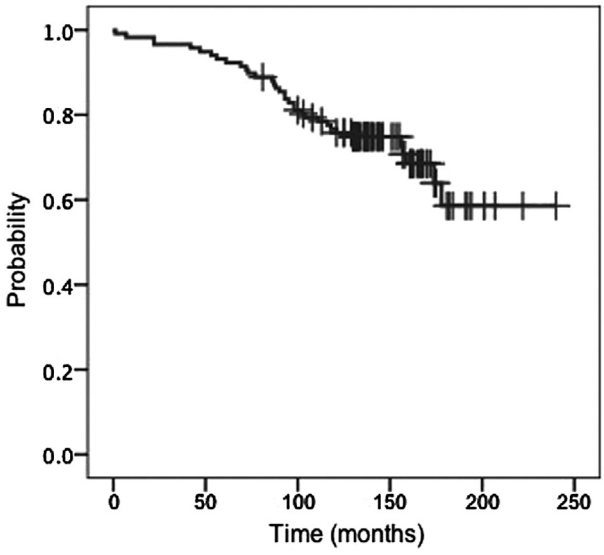

Fig. 1. Overall survival rate.

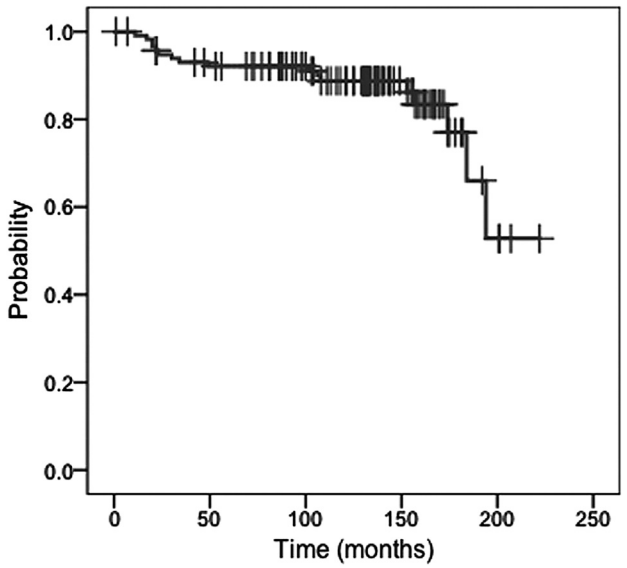

Fig. 2. Biochemical failure-free survival rate.

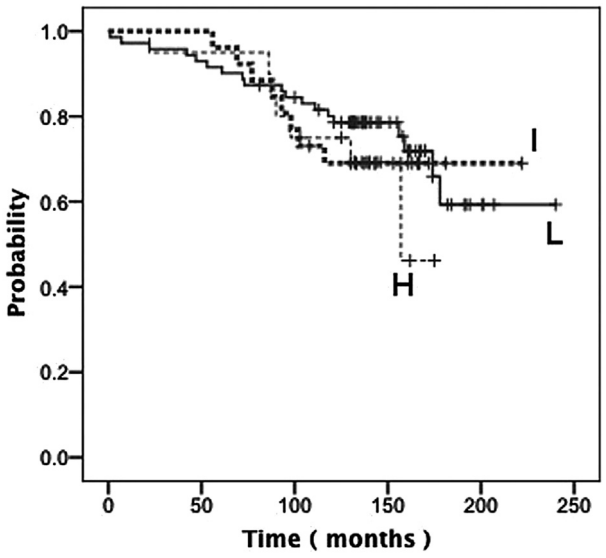

Fig. 4. Biochemical failure-free survival rate for each risk groups: low (L), Intermediate (I) and high (H). No differences between respective groups.

study.[6–8] In addition to insignificant cancer, T1c contains other tumor types, most of which may be the localized cancers that are included in the low risk group, however, approximately 17% of these cases experienced biochemical relapse within eight years after prostatectomy.[9]

Many factors have been used to discriminate among the different types of T1c tumors. Moreover, patients with localized cancer that has a mild growth tendency may be candidates for active surveillance. Ultrasonography,[10] the free-to-total PSA ratio and PSA kinetics,[11] biopsy findings and nuclear volume[12] and nomogram[13,14] are used to distinguish tumor types in localized cancers. The detection methods have been improved,[15] but these improvements do not guarantee a sharp distinction among the tumor extent.[16,17] One reason for this Inaccuracy in detection is the tumor location. Nonpalpable tumors are predominantly located in the anterior half of the gland at the apex to mid levels.[18] Magnetic resonance imaging detects tumors better than transrectal ultrasound-guided biopsy, especially in an enlarged prostate.[19] Some imaging modalities can be used to detect cancers with a volume of <0.5 cm^3.[20] Using recent technologies, however, the precise evaluation of nonpalpable prostate tumors remains to be obtained until now.

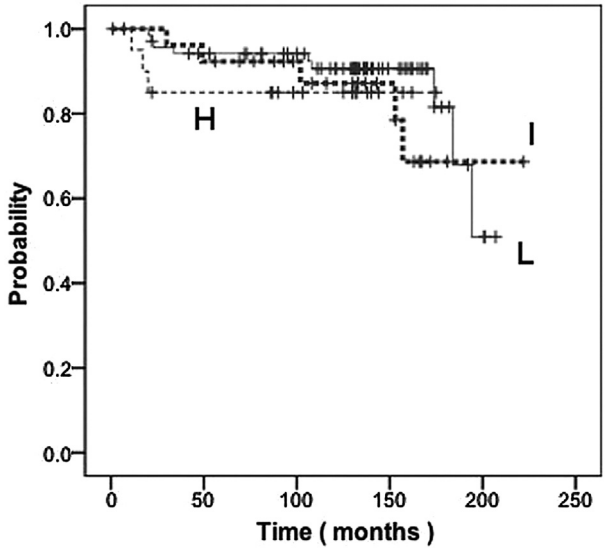

Fig. 3. Overall survival rate for each risk groups: low (L). Intermediate (I) and high (H). No differences between respective groups.

Low risk patients had a 14% rate of biochemical failure at five years under active surveillance,[21] and a 78.6% of overall survival rates at ten years.[22] With respect to their outcomes after radical prostatectomy, recent reports have shown a favorable prognosis for T2a tumors in which more than 85% and 80% of biochemical failure-free survival rates at 10 years and 15 years, respectively.[23–25]

Whether tumor properties differ between T1c and T2 is an issue for treatment. The biochemical failure-free, clinical progression-free and overall survival rates were similar for patients in both stages after radical prostatectomy.[26] However, because of the presence of invasion or high-grade prostatic intraepithelial neoplasia, T2 is a more advanced tumor.[27]

The maximum tumor volume also influences on patient outcomes: the biochemical failure-free survival rates of patients with a tumor $\leq$1.2 cm in maximum diameter showed a separation of 74.5% and 99.0% at five years after surgery.[28] Based on the probability of biochemical failure, propose has been made that patients can be divided in two groups using the following cut-off values: Gleason score of 7, 10 ng/ml of PSA and a single core biopsy containing 50% of cancer tissue. Using these parameters, the rate of freedom from PSA relapse at ten years after the operation were 96% and 73% for the low and high grades patients, respectively.[29] Similarly, low risk patients have been divided into low and very low-risk groups, resulting in more accurate prognoses: the very low risk group scarcely showed any biochemical failure.[30]

Conservative management for clinically localized prostate cancer was recommended in one study.[31] However, in another study, radical prostatectomy showed more beneficial than watchful waiting, especially for patients younger than 65 years of age.[32] For older men in the low risk group, non-curative approaches increased the risk of prostate cancer-specific mortality.[33] Radical prostatectomy resulted in a better outcome than conservative treatments, such as androgen-deprivation therapy.[34] A delay in surgery by six months or more results in a reduced progression-free survival rate in low risk patients.[35]

Combining the afore-mentioned reports with the present study, prostatectomy is one strategy for the treatment of T1c patients irrespective of various risk groups. Although radical prostatectomy has its limitations which occur in adverse effects, this treatment option may result in a favorable outcome for localized prostate cancer including T1c. Radical prostatectomy is an effective treatment option for T1c prostate cancer patients who have an expected long life span and belong to intermediate or high risk groups.

Conflicts of interest

No potential conflict of interest relevant to this article was reported.

Acknowledgments

The ethical committee of the Asahi General Hospital approved this research.

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