RESEARCH COMMUNICATION

Implications of Greater Short-term PSA Recurrence with Laparoscopic as Compared to Retropubic Radical Prostatectomy for Japanese Clinically localized Prostate Carcinomas

Hidetoshi Akita[1], Takehiko Okamura[1]*, Ryosuke Ando[1], Daisuke Nagata[2], Hiromichi Naruyama[3], Yasuyuki Yamada[3], Taku Naiki[1,2,4], Takahiro Yasui[3,4], Keiichi Tozawa[4], Kenjiro Kohri[4]

Abstract

Purpose: There is ongoing discussion as to the necessity for certain surgical procedures being limited to high through-put institutions. To cast light on this question regarding use of open as compared to laparoscopic radical prostatectomy (LRP) the present study was conducted focusing on biochemical (PSA) recurrence-free survival of Japanese patients with clinically localized prostate carcinomas. Materials and Methods: From April 2004 to December 2010 we identified 579 patients undergoing LRP (n=245) and retropubic radical prostatectomy (RRP) (n=334) who did not undergo immediate adjuvant therapy (radiation and/or hormonal) and whose PSA levels were lower than 25 ng/ml. Preoperative prostate specific antigen (PSA) level, clinical stage, biopsy Gleason score and pathological features were assessed and Kaplan-Meier estimates of biochemical recurrence (BCR)-free survival were compared. A Cox regression model analysis was performed to determine predictors of biochemical recurrence. Results: Median follow up was 35 months(2- 115). On univariate analysis the LRP group had a slightly lower pathological T stage (p<0.001), higher biopsy Gleason score (p<0.001), but much more organ confined disease (p=0.001) than the RRP group. BCR-free survival did not significantly differ between LRP and RRP groups with preoperative PSA <6, clinical stage T1c,T2a, pathological stage T3 or more, biopsy Gleason score of 8 or more, pathological Gleason score of 6 or less and 8 or more, extra-capsular extension and negative surgical margin. The 3-year BCR-free survival rates were 91.0%(RRP) and 82.2%(LRP) (p<0.001). Conclusion: We conclude that in general LRP may be associated with a less positive outcome than BCR for resection of low risk prostate cancers. Therefore indications for LRP should be very carefully monitored.

Keywords: Laparoscopic retropubic radical prostatectomy - PSA recurrence- clinically localized prostate carcinomas

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Introduction

Early detection of prostate cancer has been significantly improved, and a rapid increase in incidence has been noted in many countries during the past two decades (Sarma et al., 2002). Radical retropubic prostatectomy (RRP) provides excellent long-term disease control for patients with clinically localized prostate cancer but has a negative impact on quality of life (Hull et al., 2002). Laparoscopic surgery is an alternative which is receiving increasing attention. Initially laparoscopic surgery was used mostly for diagnostic support and for benign lesions, but it is now widely applied also for malignancies in many institutions. The first laparoscopic prostatectomy was performed in 1992, and the approach was later refined and popularized by Guillonneau and Vallencien (Guillonneau et al. 2000). Between September 1991 and May 1995, Schuessler et al. performed the first series of laparoscopic radical prostatectomy (LRP) on nine patients with clinically localized prostate cancer (Schuessler et al., 1997) and following reports of a further 10 cases in two other French institutions, this procedure has spread all over the world (Guillonneau et al., 1999, Jacob et al., 1999). Nowadays, laparoscopic radical cystectomy and urinary diversion using the gastro-intestinal tract is routine in many hospitals familiar with laparoscopic surgery. Even robotic-assisted laparoscopic surgery is now spreading worldwide. However, laparoscopic procedures

*[1]Department of Urology, JA Aichi Anjo Kosei Hospital, Anjo, [2]Department of Urology, East Medical Center Higashi Municipal Hospital City of Nagoya, [3]Department of Urology, JA Aichi Kainan Hospital, Yatomi, [4]Department of Nephro-urology, Nagoya City University, Graduate School of Medical Sciences, Nagoya, Japan *For correspondence: hiko2546@sf.commufa.jp*

are relatively difficult and it can take considerable time to obtain sufficient experience for a good outcome.

In this study, we compared laparoscopic radical prostatectomy and radical retropubic prostatectomy for clinically localized prostate carcinoma using biochemical (PSA) recurrence-free survival as the endpoint.

Materials and Methods

From April 2004 to December 2010, 630 patients with clinically localized prostate cancer underwent LRP or RRP at Nagoya City University Graduate School of Medical Sciences, East Medical Center Higashi Municipal Hospital City of Nagoya, Kainan Hospital and Anjo Kosei Hospital. From these cases, we retrospectively selected the patients with clinical T1 and T2 disease, and whose preoperative PSA level was less than 25 ng/ml. We also excluded the patients who underwent immediate adjuvant radiation therapy and/or hormonal therapy.

LRP was the intraperitoneal approach reported by Guillonneau and Vallancien as the Montsouris technique (Guillonneau et al., 2000), conducted in our institution hospitals by 16 surgeons. RRP was performed in the anatomical fashion described by Walsh and Partin (Walsh et al., 2006) with modifications by a separate group of surgeons working in hospitals where LRP facilities were not available. While the average age was lower in the LRP group, the RRP group included residents in training, so that the average level of experience was equivalent.

All specimens underwent a pathological evaluation, after fixation in 10% buffered formaldehyde with subsequent examination of paraffin-embedded sections the following day. All surgical margins and seminal vesicles were evaluated. All clinical and pathological data were entered prospectively into the registry during the above period. Stage and grade were assigned using the 1997 TNM system and the Gleason scheme, respectively ; the primary Gleason pattern was defined as the predominant portion in more than half of the specimen.

Biochemical recurrence was defined as one serum PSA level of>0.3 ng/mL and subsequent continuous elevation. Clinical local recurrence was defined as the development of a palpable nodule on digital rectal examination, or a pelvic lesion identified on CT in conjunction with a detectable serum PSA level.

The LRP and RRP groups were compared using the Wilcoxon-Mann-Whitney test and chi-square test. Biochemical recurrence (BCR)-free survival was estimated using the Kaplan-Meier method, and in all tests P<0.05 was taken to indicate significance. The data were analyzed using the SPSS statistical package (version 16; SPSS Inc., Tokyo, Japan).

Results

There were 579 patients undergoing LRP (245) and RRP(334) who met the criteria for inclusion. Median follow-up was 41 months (range 2 to 115) for the RRP group and 29 months (2 to 70) for the LRP group. There was no cancer death in our series. On univariate analysis the LRP group demonstrated slightly lower pathological

Table 1. Clinical Characteristics

		RRP (n=334)	LRP (n=245)	P-value
Mean age(range)		67.5 (46-78)	67.4 (47-82)	0.946[1]
Median ng/ml PSA		7.7 (2.6-24)	7.4 (3.1-25)	0.678[1]
Clinical T stage	T1c	187 (56.0%)	90 (36.7%)	<0.001[2]
	T2a	81 (24.3%)	86 (35.1%)	
	T2b	66 (19.8%)	69 (28.2%)	
Biopsy Gleason score	≤6	200 (59.9%)	116 (47.3%)	<0.001[2]
	7	63 (18.9%)	82 (33.5%)	
	≥8	71 (21.3%)	47 (19.2%)	
Pathological stage	pT0	13 (3.9%)	4 (1.6%)	0.001[2]
	pT2	208 (62.3%)	187 (76.3%)	
	pT3	105 (31.4%)	54 (22.0%)	
	pT4	8 (2.4%)	0 (0.0%)	
Pathological Gleason score	≤6	129 (38.6%)	82 (33.5%)	0.007[2]
	7	115 (34.4%)	115 (46.9%)	
	≥8	90 (26.9%)	48 (19.6%)	
Extracapsular extension	-ve	224 (67.1%)	194 (79.2%)	0.001[2]
	+ve	110 (32.9%)	51 (20.8%)	
Surgical margin	-ve	228 (68.3%)	144 (58.8%)	0.019[2]
	+ve	106 (31.7%)	101 (41.2%)	
Seminal vesicle invasion	-ve	323 (96.7%)	237 (96.7%)	0.985[2]
	+ve	11 (3.3%)	8 (3.3%)	

[1]Mann-Whitney U test; [2]Chi-square test; The LRP and RRP groups were compared using the Wilcoxon-Mann-Whitney test and chi-square test

Table 2. Biochemical Recurrence (BCR)-free Survival

		3-Yr BCR-Free Survival		
		RRP	LRP	p value
All		82.2	91.0	<0.001
Preoperative PSA	6 or less	92.4	92.1	0.746
	6~10	79.8	93.7	0.002
	10~25	75.7	86.4	0.036
clinical stage	T1c	86.8	92.3	0.075
	T2a	80.3	78.3	0.113
	T2b	78.3	86.2	0.066
Biopsy Gleason score	≤6	86.6	91.2	0.045
	7	76.2	94.9	0.004
	≥8	81.4	86.3	0.464
Pathological stage	T2	84.3	95.6	<0.001
	T3-4	76.4	81.7	0.336
Pathological Gleason score	≤6	91.9	93.0	0.343
	7	78.1	91.8	0.002
	≥8	73.2	86.5	0.076
Extracapsular extension	negative	83.7	95.9	<0.001
	positive	77.7	81.5	0.462
Surgical margin	negative	90.2	95.4	0.09
	positive	71.3	81.5	0.017

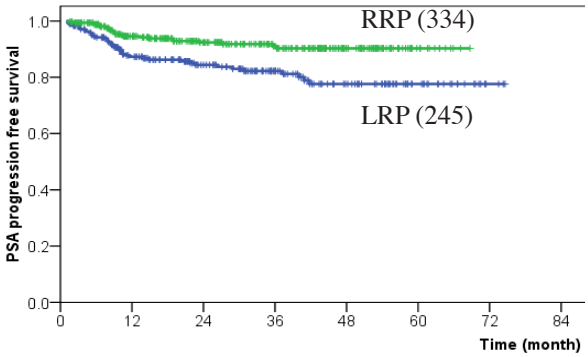

Figure 1. Biochemical Recurrence-free Survival Rates (3-year) in RRP and LRP groups Estimated using the Kaplan-Meier Method

T stage (p<0.001) and higher biopsy Gleason score (p<0.001), but much more organ confined disease (p=0.001) than the RRP group (Table 1). The BCR-free survival did not significantly differ between LRP and RRP groups with preoperative PSA <6, clinical stage T1c,T2a, pathological stage T3 or more, biopsy Gleason score of 8 or more, pathological Gleason score of 6 or less and 8 or more, extra-capsular extension and negative surgical margin (Table 2 and Figure 1).

Discussion

In our series, LRP was associated with a greater likelihood of PSA elevation than RRP. This is line with in a large scale epidemiological study from the Centers for Medicare and Medicaid Services of 2,702 men treated between 2003 and 2005, when Hu et al noted higher rates of salvage therapy necessary for patients undergoing minimally invasive RP (laparoscopic or robotic) than open RRP (adjusted OR 3.67, 95% CI 2.81–4.81) In their study, high volume minimally invasive surgeons had lower rates of re-treatment than with low volume minimally invasive surgeons (OR 0.92, 95% CI 0.88–0.98) so that experience may be an important confounding factor. Unfortunately, however, we do not have data for surgical volume with regard to either individual urologist or individual hospitals for our patients.

The most important findings in our series were that a poorer prognosis with LRP as compared RRP was linked to higher clinical T stage, higher preoperative PSA and organ-confined disease. LRP is more likely to be performed in large hospitals, possibly by younger urologists without experience of large scale series of patients. Care should therefore be taken in the future with regard to consideration of surgical indications for LRP.

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