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Outcome of Laparoscopic and Robotic Assisted Laparoscopic Radical Prostatectomy in High-risk Localized Prostate Cancer

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Abstract

Background: The treatment for high risk localized prostate cancer patients still have controversial among radiotherapy (RT), androgen deprivation therapy (ADT) and radical prostatectomy (RP).

Objectives: To study outcome of laparoscopic radical prostatectomy (LRP) and robotic assisted laparoscopic radical prostatectomy (RALP) in high risk localized prostate cancer patients.

Methods: In a retrospective descriptive analytic study from March 2005 to December 2009, 309 patients with prostate specific antigen (PSA) >20 ng/ml or Gleason score (GS) 8-10 points or Clinical T3a underwent LRP or RALP by 6 urologists. Preoperative, intraoperative and postoperative data were analyzed.

Results: The mean of age was 68.1±7.6 years old. The median of PSA was 26.27 (0.44-300) ng/ml. 48.9% of patients had GS 8-10 and 42.7% had clinical T3a. There were 61 patients (20.1%) receiving neoadjuvant ADT. 185 patients (59.8%) underwent LRP and 124 patients (40.2%) underwent RALP. The mean of operative time was 246.5±82.8 min with the median of blood loss 550 ml. (50-3,200 ml.). There was neither mortality nor converted operation to opened RP. 87 (28.3%) patients had morbidity after LRP and RALP with intraoperative complications; bleeding 17.9%, rectal injury 0.9% and nerve injury 0.3%, Postoperative complications; cardiovascular disease 10.7%, anastomotic leakage 10.4%, hematoma 3.2%, prolong lymph drainage 2.6%, bowel ileus 1.6%, pneumonia 0.9%, thromboembolism 0.3% and wound infection 0.3%. The mean of follow-up was 36.0±16.2 mo. There were late complications; anastomotic stricture 1.8% and one patient died from lung cancer. For pathological outcome, all patients had Adenocarcinoma with pGS7 47.7% and pGS8-10 47.7%.There were patients having pathological stage T3 62.3% and no lymph node metastasis 87.3%. 189 patients (61.7%) had positive margins. 5-yr Biochemical Progression-free survival (BPFS) was at 74.3%.

Conclusions: RALP is one of effective choice for treatment patients with high risk localized prostate cancer due to no mortality and minor complications.

Keywords: LRP, RALP, High risk localized prostate cancer

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Introduction

Nowadays the leading cause of death among the elderly is cancer. It was found that 25% of all newly male patients diagnosed with cancer had prostate cancer.[1] The prevalence of prostate cancer in Thailand was 75 per 10,000 people, third common, after lung cancer and colon cancer.[2] In fact, it was the second leading cause of death in male cancer.[1]

The common screening test for prostate cancer is to detect Prostate specific antigen (PSA) which is a protein produced by cells of the prostate gland. The PSA test measures the level of PSA in the blood. If PSA is high, a biopsy is usually recommended. And, the result from a prostate biopsy in the form of the Gleason score (GS) is effectively used to indicate the risk of prostate cancer patients who will have recurrent after radical prostatectomy treatment. With this diagnosis, the patients with prostate cancer are able to be detected at early stage which is considered as low risk localized prostate cancer patients. However, approximately 20-35% of the patients diagnosed with prostate cancer in early stages are considered as High risk localized prostate cancer if GS 8-10 or PSA 20 ng/dl are found.[3]

Current treatments for high risk localized prostate cancer are still controversy. The normal treatments for these patients can be radiotherapy (RT), androgen deprivation therapy (ADT) and radical prostatectomy (RP).[4] In addition, there were studies supporting that the RT combined with ADT in the treatments for these patients could control the spread of prostate cancer and reduced mortality of patients.[5] For radical prostatectomy (RP), progression free survival at 5 and 10 years was 55% and 36%, respectively.[6,7] Furthermore, only RP can decrease biochemical failure (BCF) and spread of cancer more than RT alone.[8] Treatment with ADT before surgery did not reduce the spread of prostate cancer after surgery.[9]

The endoscopic surgery is now widely recognized and acceptable in term of less complications following surgery for prostate cancer patients. There are two endoscopic surgeries: Laparoscopic radical prostatectomy (LRP) and robotic assisted laparoscopic radical prostatectomy (RALP).[10] To reduce complications of surgery and unsatisfied pathological outcome in surgical treatment for high risk localized prostate cancer patients, the appropriate patients should be carefully selected.[4]

However, there were only few studies on outcomes and complications after endoscopic surgery in high risk localized prostate cancer.[10-16] The lack of information on endoscopic surgery study affects to the medical decision on the treatment for the patients. Therefore, this study emphasized the outcome of prostate endoscopic surgery in patients with high risk localized prostate cancer to evaluate the effectiveness on this treatment.

Material & Methods

The present study is a descriptive and analytical retrospective in patients who underwent endoscopic surgery for prostate cancer (LRP or RALP) at Siriraj Hospital from March 2005 to December 2009. The study has been approved by the ethics committee in human research. Inclusion criteria were patients who have been diagnosed with prostate cancer with PSA >20 ng/mL or GS = 8-10 points or clinical T3a. Patients who had a prior abdominal surgery were excluded. Preoperative, intraoperative and postoperative patient data were from medical records. Before surgery, the patients were physically and digital rectal examined. Also, the basis of blood tests, the chest x-ray, and the electrocardiography were used to evaluate the patients before surgery. Besides, some patients were diagnosed with the bone scan or the computer tomography whole abdomen to evaluate the stage of prostate cancer.

An endoscopic surgery for each patient was performed by one urologist. This study observed the outcomes from the surgeries from 6 urologists who had performed the surgeries in standard techniques; Extraperitoneal and Transperitoneal approaches. Both techniques were preferably selected by each surgeon.

Before surgery, some patients received Neo-adjuvant ADT which comprise of Ganadotropic-releasing hormone (GnRH) agonist and antiandrogen.

After surgery, the morbidity and mortality in postoperative patients were studied in three phases; intraoperative, postoperative and late phases which were related to the operating conditions. Moreover, some patients who had biochemical failure (PSA > 0.2 ng/ml) or unsatisfied pathological outcome and received the other treatments (ADT and/or RT) after surgery were observed in this study.

The descriptive statistic in SPSS program version 15.0 was used to describe the findings in this study. The comparison on the results of the data from the investigation between both LRP and RALP used Independent t-test, Mann Whitney-U test for continuous data and statistics, and Chi-square test or Fisher's exact test for group data. To determine the effect of complications after surgery, Kaplan-Meier method for Biochemical Progression-free survival after surgery was used.

Result

There were 309 patients who had high risk localized prostate cancer underwent LRP and RALP. In total there were 185 patients (59.8%) received LRP and 124 patients (40.2%) received RALP regarding to the basis patient's characteristic as Table 1.

No significant difference in the characteristics of basis patients in both groups was found. And, the laboratory tests of all patients in this study were normal with no statistical difference on the results between LRP and RALP. Exceptionally, the patients with stroke were found more common in RALP group (*p-Value* = 0.049).

There were 61 patients (20.1%) receiving the Neoadjuvant ADT, 22 patients (7.1%) receiving the GNRH agonist and Antiandrogen, 20 patients (6.5%) receiving the GNRH agonist alone, and only 19 patients (6.1%) receiving the Antiandrogen.

Based on the analysis in this group of patients, it showed that receiving neoadjuvant ADT was not related to recurrence after surgery (*p-Value* = 0.154) and did not effect on the margin of the pathology (*p-Value* = 0.496).

The operative data was shown in Table 2. Extraperitoneal approach was used in 135 patients (44.0%) and transperitoneal approach was used in 172 patients (56.0%). The transperitoneal approach was used in RALP group more than LRP group (*p-Value* <0.001). The average operative time considering in both RALP and LRP was 246.5±82.8 minutes. In comparison, the average operating time in RALP group was less than the LRP group (*p-Value* <0.001). The average of blood loss amount during surgery in total was 550 ml (50-3,200 ml). In Transperitoneal approach patients, RALP group had blood loss during surgery less than LRP group (*p-Value* <0.001). Thus, patients in RALP group received less blood than LRP group (*p-Value* <0.001). In the group receiving extraperitoneal approach, blood loss between LRP and RALP group was not different (*p-Value* = 0.062). However, the average of receiving blood amount in total; 505.0±237.3 ml, was not different from the amount in both RALP and LRP alone (*p-Value* = 0.971).

In this study, there was no patient who was needed to be converted to open abdominal surgery. And none of the patients died immediately after surgery. The 76 patients (24.8%) were in the ICU unit for 1-2 days after surgery. Afterwards, the

Table 1 *Basis patient's characteristics.*

		LRP	RALP	Total
Age (years) - Mean±SD		67.4±7.3	69.0±8.0	68.1±7.6
Body weight (Kg) - Mean±SD		67.0±11.0	37.0±11.0	67.0±11.0
Height (Cm) - Mean±SD		165.0±7.0	166.0±6.0	165.0±7.0
PSA (ng/dL) - Median (Min - Max)		25.54 (0.44-227)	27.3 (1.6-300)	26.27 (0.44-300
Gleason score*	7	47 (26.3%)	51 (41.1%)	98 (32.3%)
	8	66 (36.9%)	19 (15.3%)	85 (28.1%)
	9	32 (17.9%)	22 (17.7%)	54 (17.8%)
	10	8 (4.5%)	1 (0.8%)	9 (3.0%)
Clinical T3a		85 (46.4%)	46 (37.1%)	131 (42.7%)
Smoking		49 (26.6%)	29 (24.0%)	78 (25.6%)
Alcohol drinking		30 (16.2%)	16 (13.2%)	46 (15.0%)
Underlying disease	Hypertension	102 (55.1%)	74 (59.7%)	176 (57.0%)
	Diabetic mellitus	33 (17.8%)	29 (23.4%)	62 (20.1%)
	Dyslipidemia	32 (17.3%)	26 (21%)	58 (18.8%)
	Colonary artery disease	17 (9.2%)	9 (7.3%)	26 (8.4%)
	Stroke*	2 (1.1%)	8 (6.5%)	10 (3.2%)
Normal	Chest X-ray	160 (86.5%)	116 (93.5%)	276 (89.3%)
	Electrocardiography	146 (78.9%)	93 (75.0%)	239 (77.3%)
ASA Classification	1	18 (9.7%)	14 (11.3%)	32 (10.4%)
	2	151 (81.6%)	96 (77.4%)	247 (79.9%)
	3	16 (8.6%)	14 (11.3%)	30 (9.7%)
Neoadjuvant ADT		40 (21.6%)	21 (17.7%)	61 (20.1%)
Preoperative Incontinence	None	154 (99.4%)	89 (98.9%)	243 (99.2%)
	Pad = 1/Day	1 (0.6%)	1 (1.1%)	2 (0.8%)
	Pad >1/Day	0	0	0
Preoperative Potency	Impotence	24 (17.9%)	2 (25.0%)	26 (18.3%)
	Partial Potency	27 (20.1%)	1 (12.5%)	28 (19.7%)
	Fully Potency	83 (61.9%)	5 (62.5%)	88 (62.0%)

*p-*Value* < 0.05

patients were able to be transferred to the ward under routine care.

After operation, the median postoperative hospital stay was 7 days (3-36 days), and the median duration of drainage was 4 days (1-30 days). Also, the median duration of urethral catheterization was 8 days (6-93 days). Likely, the hospital stay, the duration of drainage, and the duration of urethral catheterization were less in RALP group than LRP group (*p-Value* <0.05).

The results of complications during surgery and after surgery are shown in Table 3. The Rectal injury condition was found in three patients (0.9%), which two patients had received extrapertitoneal approach LRP and one patient had received transperitoneal approach LRP. All of them had never received Neoadjuvant ADT. Only one patient who had received extraperitoneal approach LRP had nerve injury (0.3%).

The most postoperative complications after LRP and RALP were cardiovascular disease at 10.7%, followed by anastomotic leakage at 10.4% and hematoma at 3.2% of all patients. And, the complications of cardiovascular disease, anastomotic leakage, and hematoma were found in LRP group more than RALP (*p-Value* < 0.05). However, there was no correlation between extraperitoneal and transperitoneal approach causing the occurrence of all complications found in LRP and RALP group (*p-Value*> 0.05).

For the postoperative cardiovascular disease complications, there were only 5 ST-elevate myocardial infarction (STEMI) patients (1.6%). And, the rest which was 9.1% of all patients were non STEMI, Arrhythmia, Atrial fibrillation (AF), Premature ventricular contraction (PVC), and Premature atrial contraction (PAC). All of patients who had cardiovascular complications were treated by cardiologist until clinical relieved. Other conditions were observed, such as

Table 2 *Surgical Data of LRP and RALP in High Risk Localized Prostate Cancer.*

		LRP	RALP	Total
Approach*	Extraperitoneum	117 (63.9%)	18 (14.5%)	135 (44.0%)
	Transperitoneum	66 (36.1%)	106 (85.5%)	172 (56.0%)
Nerve Sparing	None	157 (86.3%)	107 (86.3%)	264 (86.3%)
	Unilateral	10 (5.5%)	3 (2.4%)	13 (4.2%)
	Bilateral	15 (8.2%)	14 (11.3%)	29 (9.5%)
Length of Operation* (min) - Mean±SD		266.5±74.1	216.0±86.3	246.5±82.8
Blood Loss* (ml) - Median (Min - Max)		650 (50-3200)	400 (50-2600)	550 (50-3200)
Blood Transfusion	Yes	53 (28.6%)	11 (8.9%)	64 (20.7%)
	Amount (ml) Mean±SD	505.5±246.4	502.0±199.7	505.0±237.3
ICU admission*		56 (30.6%)	20 (16.1%)	76 (24.8%)
Foley catheter* (Day) - Median (Min -Max)		8 (6-43)	8 (6-93)	8 (6-93)
Drain* (Day) - Median (Min - Max)		4 (1-30)	3 (2-11)	4 (1-30)
Hospital Stay* (Day) - Median (Min - Max)		8 (3-36)	7 (3-13)	7 (3-36)
Follow-up (Months) - Mean±SD		39.2±17.9	31.2±12.0	36.0±16.2

*p-*Value* < 0.05

Table 3 *Complications of LRP and RALP in High Risk Localized Prostate Cancer.*

		LRP	RALP	Total
Complication		66 (36.1%)	21 (16.9%)	87 (28.3%)
Intraoperation	Hemorrhage*	42 (22.7%)	13 (10.5%)	55 (17.9%)
	Rectal Injury	3 (1.6%)	0	3 (0.9%)
	Nerve Injury	1 (0.5%)	0	1 (0.3%)
Postoperation	Cardiovascular Disease*	25 (13.5%)	8 (6.5%)	33 (10.7%)
	Anastomotic Leakage*	23 (12.4%)	9 (7.2%)	32 (10.4%)
	Hematoma*	10 (5.4%)	0	10 (3.2%)
	Prolong Lymph Drainage	2 (1.1%)	6 (4.8%)	8 (2.6%)
	Bowel Ileus	1 (0.5%)	4 (3.2%)	5 (1.6%)
	Pneumonia	3 (1.6%)	0	3 (0.9%)
	Thromboembolism	1 (0.5%)	0	1 (0.3%)
	Wound Infection	0	1 (0.8%)	1 (0.3%)
Postoperative Incontinence	None	53 (34.9%)	68 (77.2%)	121 (50.4%)
At 6 months	Pad = 1/d	44 (28.9%)	13 (14.8%)	57 (23.8%)
	Pad > 1/d	55 (36.2%)	7 (8.0%)	62 (25.8%)
Postoperative Potency	Impotence	122 (91.0%)	3 (50.0%)	125 (89.3%)
At 6 months	Partial Potency	11 (8.2%)	3 (50.0%)	14 (10.0%)
	Full Potency	1 (0.7%)	0	1 (0.7%)

*p-*Value* < 0.05

prolong lymph drainage (2.6%), bowel ileus (1.6%), pneumonia (0.9%), thromboembolism (0.3%), and wound infection (0.3%). No patients had complication with renal or Incisional hernia after surgery. Additionally, the urinary incontinence and the erection potency at 6 months after surgery of the patients who underwent the surgery were found at 49.6% and at 89.3%, respectively.

The pathological outcomes are shown in Table 4. All patients in this study had adenocarcinoma cancer which most of patients had Gleason score 7; accounting for 47.7% of all patients. And, the pathological positive margin was found in 189 patients (61.7%) which were no significant difference between LRP and RALP groups (p-*Value* = 0.383). The numbers of patients having pathologic T3 (pT3) were 188 (62.3%). However, the overdiagnosis was found which 27 patients (28.7%) actually had pathologic T2 (pT2). There were 269 patients (87.3%) who had no tumor spreading to lymph nodes.

The percentage of all patients who had 5 year-biochemical progression-free survival (BPFS) was at 74.3% (Figure 1). Pathological Gleason Score (pGS) after surgery showed that pGS7, pGS8 and pGS9 with 5- year BPFS were 76.9%, 63.2% and 62.5%, respectively (Figure 2). After surgery, 164 patients (54.5%) received hormone therapy immediately. Among these patients, there were 119 patients (62.9%) with a Positive margin and 45 patients (38.5%) with Negative Margin.

The selected patients received other treatments after surgery as shown in Table 5. There was only

one patient who died due to prostate cancer after surgery (0.3%). And, only one patient required chemotherapy because of the condition of hormonal castration resistant prostate cancer.

In the patient group of PSA rising after operation, there were 46 patients (15.2%). In this group, there were 24 patients (52.2%) in the positive margin and 22 patients (48.8 %) in the negative margin. And, all patients in PSA rising group were treated with ADT and RT, as shown in Table 5. The pathological margin was not a factor related to the rise of PSA after surgery (*p-Value* = 0.444).

The late complication was found in six patients (1.8%) with anastomotic stricture. Among these patients, there was one patient who had pyelonephritis because of anastomotic stricture. And, there

Table 4 *Pathological Outcome.*

		LRP	RALP	Total
pT3	pT3a	51 (28.3%)	30 (24.6%)	81 (26.8%)
	pT3b	65 (36.1%)	42 (34.4%)	107 (35.4%)
	pT4	6 (3.3%)	6 (4.9%)	12 (4.0%)
pNode	pN0	163 (88.6%)	106 (85.5%)	269 (87.3%)
	pN1	16 (8.7%)	7 (5.6%)	23 (7.5%)
Margin	Negative	75 (41.0%)	42 (34.1%)	117 (38.3%)
	Solitary Positive	56 (30.6%)	46 (37.4%)	102 (33.3%)
	Multiple Positive	52 (28.4%)	35 (28.5%)	87 (28.4%)
Gleason Score	7	82 (45.3%)	63 (51.2%)	145 (47.7%)
	8	34 (18.8%)	21 (17.1%)	55 (18.1%)
	9	53 (29.3%)	35 (28.5%)	88 (28.9%)
	10	2 (1.1%)	0	2 (0.7%)
PSA Rising	n(%)	25 (13.8%)	21 (17.2%)	46 (15.2%)

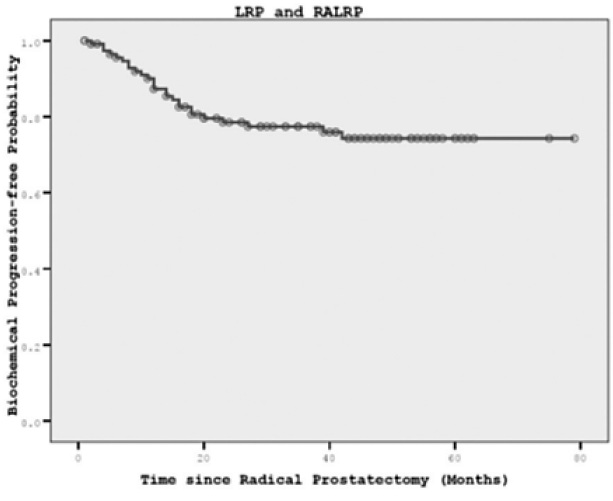

Fig 1 *Biochemical Progression-free survival.*

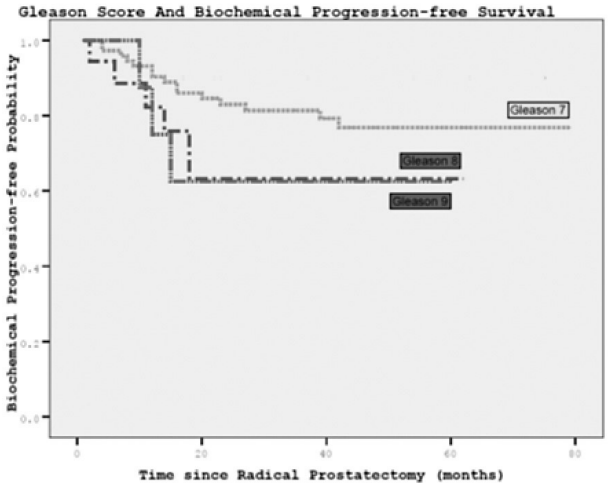

Fig 2 *Gleason score and Biochemical Progression-free survival.*

Table 5 *Immediate Adjuvant Therapy and Adjuvant Therapy.*

	LRP		RALP		Total
Adjuvant Therapy	**Immediate**	**Late**	**Immediate**	**Late**	
Bilateral Orchiectomy	31 (33.7%)	6 (31.6%)	2 (2.8%)	0	39 (19.2%)
GnRH agonist	49 (53.3%)	8 (42.2%)	57 (79.2%)	14 (70%)	128 (63.1%)
Antiandrogen	26 (28.3%)	7 (36.8%)	37 (51.4%)	10 (50%)	80 (39.4%)
Radiation Therapy	6 (6.5%)	5 (26.3%)	17 (23.6%)	3 (15%)	31 (15.3%)
Chemotherapy	0	1 (5.3%)	0	0	1 (0.5%)

was one patient who died from lung cancer which had been diagnosed after operation.

Discussion

Current treatments for high risk localized prostate cancer have no conclusions. Thus, the means of endoscopic surgery in these patients may be the options for cancer treatment because these methods are safe and lead to less complications.[10] There are few studies of outcomes and complication of laparoscopic surgery in high risk localized prostate cancer.[10-16] According to the research by Rassweiler et al10 found that there was no mortality after surgery and found the rate of change of laparoscopic surgery to open surgery of 2.4%. Similarly, this study showed that there was no mortality due to endoscopic surgery and no rate of change of endoscopic surgery to open surgery was found.

Complications rate after surgery of the Rassweiler et al[10,11] study was found at 12.3%, but in this study the rate was found at 28.3% which found intraoperative complications more than in the postoperative complications. Intraoperative complication which was mostly found was the incidence of bleeding. The possible cause was from the spread of cancer outside the tumor mass which made more difficulty in the operation. And, Rassweiler et al study did not specify in the patients with high risk localized prostate cancer unlike this study. These probably cause different numbers of complications in both studies.

The postoperative complication found major cardiovascular complication at 0.1% in studies of Rassweiler et Al[10,11] and 1.6% in this study. Furthermore, minor cardiovascular complication was 9.1% of patients in this study. Although there were high numbers of patients who had cardiovascular complications, all these patients were cared by Cardiologist until they discharged. And, there was no mortality from cardiovascular complications.

Anastomotic leakage was found to 10.4% when compared with studies of Rassweiler et Al[10,11] that found only 0.2%. The possible cause of high anastomotic leakage in the study was that the patients were performed with cystography before removing the urethral catheter. The cystography was done at 6 days after surgery. However, the contrast leakage patients in this study had no symptoms. If contrast leakage was found, the patients had to be followed up about 2 weeks after surgery and took off the urethral catheter. Only two patients (0.6%) required a urinary catheter for 43 days and 93 days because of anastomotic leakage.

Minor complications with a high risk localized prostate cancer in this study were the same as found in studies of Rassweiler et Al.[10,11] Hence, the

secure on surgery for the patients in high risk localized prostate cancer were considered as same as the patients in intermediate and low risk localized prostate cancer.

The urinary continent from the study of Rasweiler et al[11] found that the continent rate (no pad) was 84.9% at 12 months after surgery. However, this study showed that it was 50.6% at 6 months after surgery, which if the follow up were at 12 months, the rate in this study would be improved.

The study of the erection potency after the surgery in this study show that patients with impotence were found at 89.3% which were higher than the patients in the study of Rasweiler et al.[11] As the patients in this study were considered as high risk recurrence after surgery, the surgeon chose not to keep the cavernous nerves of the patients. This study had non-nerve sparing patients at 86.3% which these patients should have higher chance of impotency. Due to a relatively small numbers in nerve sparing patients, it is impossible to analyze the results.

Based on the pathology of the prostate, there were 28.7% of patients receiving overdiagnosis to be the stage of clinical T3a disease instead of pT2. Generally speaking, patients in this group possibly may be treated by RT, ADT, or combination of both which they actually should have surgery to remove the tumor completely.

Oncological results from the study of Rasweiler et al[11] found that the patients in pT2 and pT3 had positive margin at 10.6% and 32.7% and PSA-recurrence at 8.6% and 17.5%, respectively. And from the study of Tse et al found that the patients in high risk catagories had positive margin rate at 63%.[12] In this study showed that the patients in pT2 and pT3 had positive margin at 46.1% and 70.6% and PSA-recurrence at 19.2% and 13.5% respectively. The oncological results in this study which were higher rate than the previous study were likely caused by the learning period of LRP and RALP, which made higher amount of time and positive margin.

5-year BPFS found in the patients in this study was at 74.3%. Incidentally, the studies of Koupparis et al[13], Spahn et al[14] and Touijer et al[15] found that 5-year BPFS was at 76%, 64.8% and 53% respectively. Although this study had higher margin positive rate than other studies, the study of Lewinshtein et al claimed that there was no effect of positive margin on BPFS.[16]

Conclusion

The endoscopic surgery in high risk localized prostate cancer is safe to be used with no mortality and low morbidity after surgery. Referring to the study, RALP caused fewer complications than LRP. Thus, this may be an alternative effective treatment for these patients.

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