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Relationship of Positive Resection Margin, Cancer Location and Learning Curve after Laparoscopic Radical Prostatectomy

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Abstract

Background: One of surgical goals is decreasing of positive resection margin (PRM). In radical prostatectomy, PRM is important because of prognostic factor. We examine the relationship of PRM, cancer location and learning curve after laparoscopic radical prostatectomy (LRP).

Methods: Between May, 2009 and May, 2015, 331 consecutive patients were treated with LRP. The resection margin status, Gleason score, pathological stage, cancer location and diameter were assessed in each surgical specimen, and the independent factors for PRM and prostate-specific antigen (PSA) failure were identified. The learning curve for PRM was calculated and the number of cases until the plateau was obtained.

Results: PRM was found in 30.5% of all patients, with 27.7% in the pT2 patients and 39.0% in the pT3 patients. The most common site of PRM was in the apex-anterior. The 5-year PSA failure-free survival rate was 73.9%. In patients with a negative resection margin, the 5-year PSA failure-free survival rate was 81.6%, and in patients with PRM, it was 57.4%. The factors associated with PSA failure-free survival were PRM and elevated PSA. The tumor location was not associated with PSA failure-free survival. The factors associated with PRM were tumor location, nerve sparing procedure, and tumor diameter. When the tumor was localized in the apex-anterior, the rate of PRM was elevated 3-fold comparing the tumor in apex-posterior. The learning curve of all surgeons for obtaining a negative resection margin plateaus after 167 cases. The curve of a single surgeon was more improved than all surgeons and the rate of PRM was 16.7%.

Conclusions: PRM was associated with both cancer location and diameter. The learning curve of PRM reached a plateau in about 170 cases. However, PRM can be further reduced. These findings related to LRP outcomes are useful for improvement in surgical techniques and for determining prognosis.

Keywords: Laparoscopic radical prostatectomy; Positive resection margin; Cancer location; PSA failure; Learning curve

Introduction

Laparoscopic radical prostatectomy (LRP) was developed in Europe in the late 1990s and was established as in important surgical treatment [1-3]. LRP was initially compared with retropubic radical prostatectomy (RRP), and the oncological outcome was equal to that of RRP [4]. Subsequently, the LRP surgical technique was improved, and it was used worldwide. The benefit of LRP with pneumoperitoneum was that it allowed both a magnified view of the surgical area and a clear surgical space. However, LRP was not routinely used in Japan for prostate surgery because the technique was difficult and Japanese facilities need to acquire the authorization on starting this operation [5,6].

Recently, the long-term results of LRP were reported, including a study by Hruza et al on 370 patients [7-10]. According to this report, the 10-year cancer specific survival (CSS) rate was 100% in pT2 patients, 97.3% in pT3a patients, and 90.6% in pT3b/4 patients after a median observation period of 105 months. They also reported that the prostate-specific antigen (PSA) recurrence-free survival rate were 80.2%, 47.4%, 49.8%, respectively for pT2 (Tumor confined within prostate), pT3a (extraprostatic extension), and pT3b/4 (Tumor invades seminal vesicle/the bladder, external sphincter) patients. In contrast, our study examined the tumor location, positive resection margin (PRM), and PSA failure among RRP-treated patients previously [11]. We found that a PRM was most common with an apex tumor and apex tumor had worse prognosis. For LRP, the tumor location and PRM were as important as RRP for the oncological outcome.

In this study, we examined the cancer location and PRM for LRP, identified prognostic factors for PRM and PSA failure, and discussed the learning curve for performing LRP.

Patients and Methods

We performed LRP on 352 patients between May, 2009 and May, 2015. Among them, 21 patients were excluded from the study because of neoadjuvant hormone therapy. The remaining 331 patients were enrolled in this study. Our surgical procedure was described previously

[12]. Briefly, the procedure was performed with an extraperitoneal and antegrade approach. Only 2 patients received an LRP by the intraperitoneal approach because of a large tear in the peritoneum during the surgery. All patients were performed lymph node dissections and it was limited within obturator fossa. After reconstruction of the posterior structure, a vesicourethral anastomosis was performed with a running suture. All LRP procedures were performed by the same surgeon (K.H.) or by the surgeon's team in his presence. Based on the location and Gleason score of the biopsy, nerve sparing procedure was decided whether to preserve either both sides, one side or none.

The pathological evaluations were also described previously [11]. Briefly, all hematoxylin–eosin pathological slides of the radical prostatectomy specimens were reviewed. The Gleason score, pathological stage, tumor location, tumor diameter and resection margin status were assessed in each surgical specimen based on the WHO guideline. A PRM was defined as the presence of tumor cells at the resection margin. The largest (here termed primary) and second largest (here termed secondary) tumors were assessed to determine if multiple tumors were present. No other tumors from lesions with multiple tumors were analyzed if there were no specific findings. The prostate was divided into three equal parts, including the apex, middle, and base. A tumor in the apex-anterior was defined as the lesion above the urethra, and a tumor in the apex-posterior was defined as the lesion inferior to the urethra.

All patients were evaluated at 1- to 3-month intervals after surgery by PSA measurements for 5 years, and biannually thereafter. PSA recurrence was defined as a PSA 0.2 ng/ml. If the PSA was not <0.2 ng/ml after surgery, PSA recurrence was defined at the day of surgery. Imaging studies, including computed tomography, magnetic resonance imaging, and radioisotope bone scans, were carried out only after either PSA recurrence or clinical disease progression.

The χ^2-test and Kruskal–Wallis test were used to evaluate the clinical and pathological parameters. PSA recurrence-free survival was examined using the Kaplan–Meier method and analyzed by the log–lank test. A Cox proportional hazards model was used to assess the risk of PSA recurrence, and a logistic regression model was used to assess the relationship of PSA recurrence with both PRM and clinical factors. In multivariate analysis, PSA, age, Gleason score, tumor diameter, and years at surgery were used as continuous parameters, and resection margin (positive vs. negative), primary and secondary tumor locations and site of PRM (apex-anterior, apex-posterior, middle, base), nerve sparing surgery (with vs. without), pathological stage (pT2 vs. pT3), and pN (pN0 vs. pN1) were used as categorical parameters. Learning curves were obtained by cubic splines. The level of significance was taken to be $P<0.05$ in all analyses. This study was approved by the Institutional Review Board.

Results

The median age of the patients was 67.0 years, and the PSA median was 7.50 ng/ml. There was no patient with open conversion. Forty-seven patients had a preserved neurovascular bundle. The median observation period was 48.1 months for surviving patients. None of the patients died due to prostate cancer. Four patients died without prostate cancer during the 26.9-month follow-up periods. Among the 331 patients, 249 patients were pT2, and 82 patients were pT3. The backgrounds of the patients based on pathological stage are listed in Table 1. Age and prostate weight were the same in both groups. However, other pathological factors, such as tumor diameter, Gleason score, PRM, and lymph node metastasis were significantly worse in the pT3 group. The primary tumor diameter was 1.6 cm in all cases. The primary tumor was larger in the pT3 group when compared with that in the pT2 group. But, the secondary tumor was not different in size between the pT2 and pT3 groups. A PRM was found in 30.5% of all patients, with a 27.7% occurrence in the pT2 patients and a 39.0% occurrence in the pT3 patients. Lymph node metastasis was found in 2.7% of all cases, and 9.8% occurred in the pT3 patients. Extra-prostatic extension (EPE) in the pT2 patients was localized to the side of the bladder.

	All	pT2	pT3	P value*
Number	331	249	82	
Age (years)	67.0 (50-79)	67.0 (51-76)	67.0 (50-79)	0.226
PSA (ng/ml)	7.50 (1.66-74.46)	6.99 (1.66-31.72)	11.93 (3.61-74.46)	<0.001
BMI	23.9 (17.0-32.7)	23.8 (17.0-32.7)	24.6 (17.3-30.9)	0.040
Prostate weight (g)	45 (20-105)	45 (20-105)	50 (20-100)	0.495
Primary tumor diameter (cm)	1.6 (0.1-4.3)	1.5 (0.1-4.0)	2.2 (0.5-4.3)	<0.001
Secondary tumor diameter (cm) (n302)	0.8 (0.1-2.5)	0.7 (0.1-2.1)	0.8 (0.1-2.5)	0.040
Primary + secondary tumor diameter (cm)	2.4 (0.1-5.8)	2.2 (0.1-4.9)	3.2 (0.9-5.8)	<0.001
Gleason score (-6/7/8-)	40/199/92	39/163/47	1/36/45	<0.001
Positive resection margin (%)	101 (30.5)	69 (27.7)	32 (39.0)	0.072
EPE (%)	64 (19.3)	2 (0.8)**	62 (75.6)	<0.001
pN1 (%)	9 (2.7)	1 (0.4)	8 (9.8)	<0.001
Nerve sparing (%)	47 (14.2)	42 (16.9)	5 (6.1)	0.017

BMI; body mass index, EPE: extraprostatic extension; *: pT2 vs pT3, **: EPE was localized to the side of the bladder

Table 1: Background parameters by pathological stage.

Information on the primary tumor location and on the PRM is presented in Table 2. Two-thirds of primary tumors were localized in the apex. A PRM was found in 23.6% of the primary tumors, and apex-anterior was most common site. The locations of the primary tumors were almost equally distributed between the apex-anterior and -posterior, but the PRM in the apex-posterior was low compared to that in the apex-anterior. The PRM in the pT2 patients was low compared to that in the pT3 patients. The most common site of a PRM was the apex-anterior in the pT3 patients. The occurrence of a PRM in the pT3 patients was high for all locations, especially the base site when compared with that of the pT2 patients. Secondary tumors were found in 302 of the cases. The PRM was 10.3% in all secondary tumors, and the frequency was same in both the pT2 and pT3 patients. The apex-anterior was most common site for secondary tumors, but the frequency was low when compared to that of the primary tumors (Table 3).

Location	All		pT2		pT3	
	number	PRM (%)	number	PRM (%)	number	PRM (%)
Apex-anterior	96	44 (45.8)	80	33 (41.8)	16	11 (68.8)
Apex-posterior	106	20 (18.9)	78	11 (14.1)	28	9 (32.1)
Middle	110	6 (5.5)	84	4 (4.8)	26	2 (7.7)
Base	19	8 (42.1)	7	1 (14.3)	12	7 (58.3)
Total	331	78 (23.6)	249	49 (19.7)	82	29 (35.4)
P value		<0.001		<0.001		<0.001
PRM: positive resection margin						

Table 2: Primary tumor location and positive resection margin in pT2 and pT3 cases.

The 5-year PSA failure-free survival rate was 73.9%. For patients with a negative resection margin, it was 81.6%, and for those with a PRM, it was 57.4% (Figure 1). The factors associated with PSA failure were PRM and PSA level. Tumor location was not associated with PSA failure in all cases. Among the pT2pN0 patients, the factors associated with PSA failure were the same in all cases, but among the pT3 patients, the pathological stage and tumor location were independent factors. The PRM at the base site in pT3b patients indicated a worse prognosis in the pT3pN0 patients (Table 4). The factors associated with a PRM were tumor location, nerve sparing procedure, and tumor diameter. In the pT2 patients, the factors were the same, but in the pT3 patients, the tumor diameter was not an independent factor (Table 5).

Location	All		pT2		pT3	
	number	PRM (%)	number	PRM (%)	number	PRM (%)
Apex-anterior	80	18 (22.5)	61	14 (23.0)	19	4 (21.2)
Apex-posterior	78	7 (9.0)	60	5 (8.3)	18	2 (11.1)
Middle	137	4 (2.3)	97	3 (3.1)	40	1 (2.5)
Base	7	2 (28.6)	6	1 (16.7)	1	1 (100)
Total	302	31 (10.3)	224	23 (10.3)	78	8 (10.3)
P value		<0.001		<0.001		<0.001
PRM: positive resection margin						

Table 3: Secondary tumor location and positive resection margin in pT2 and pT3 cases.

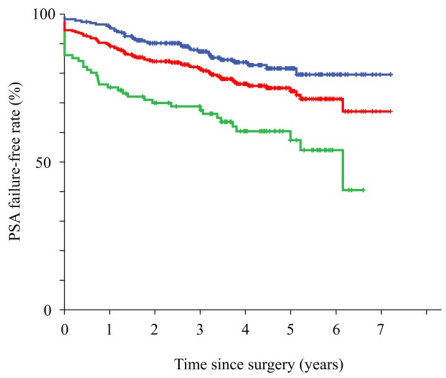

Figure 1: PSA failure-free survival relative to the resection margin. Red: all cases, blue: negative resection margin, green: positive resection margin.

	All (n=331)		pT2pN0 (n=248)		pT3pN0 (n=74)	
	HR	P value	HR	P value	HR	P value
Resection margin (negative vs. positive)	2.61 (1.57-4.37)	<0.001	3.07 (1.57-6.02)	0.001	2.69 (1.09-6.64)	0.032
PSA (range)	1.03 (1.00-1.05)	0.022	1.07 (1.01-1.14)	0.020	-	-

Cancer location			-			
(2 vs. 1)	1.14 (0.64-2.05)	0.651	1.45 (0.62-3.36)	0.388	0.83 (0.34-2.06)	0.691
(3 vs. 1)	0.90 (0.46-1.73)	0.743	0.87 (0.35-2.11)	0.750	0.64 (0.19-2.10)	0.457
(4 vs. 1)	0.42 (0.16-1.09)	0.075	1.52 (0.43-5.35)	0.519	0.08 (0.01-0.45)	0.004
Pathological stage (pT3a vs. pT3b)	-	-	-	-	3.463 (1.61-7.44)	0.001
1: apex-anterior, 2: apex-posterior, 3: middle, 4: base						

Table 4: Multivariate analysis for PSA recurrence in all cases, pT2pN0 and pT3pN0 cases.

	All (n=331)		**pT2pN0 (n=248)**		**pT3pN0 (n=74)**	
	HR	**P value**	**HR**	**P value**	**HR**	**P value**
Tumor diameter (primary)	2.60 (1.78-3.78)	<0.001	2.08 (1.22-3.54)	0.007	4.82 (1.72-13.49)	0.003
Tumor location (primary)						
2 vs. 1	2.82 (1.49-5.32)	0.001	3.21 (1.52-6.76)	0.002	2.75 (0.56-13.33)	0.211
3 vs. 1	5.29 (2.60-10.75)	<0.001	3.95 (1.80-8.70)	<0.001	35.71 (2.99-500)	0.005
4 vs. 1	0.95 (0.33-2.74)	0.924	2.48 (0.42-14.29)	0.318	0.38 (0.05-2.99)	0.360
Nerve sparing (no vs. yes)	3.33 (1.54-7.16)	0.002	2.81 (1.26-6.30)	0.012	-	-
1: apex-anterior, 2: apex-posterior, 3: middle, 4: base						

Table 5: Multivariate analysis of factors associated with positive resection margin.

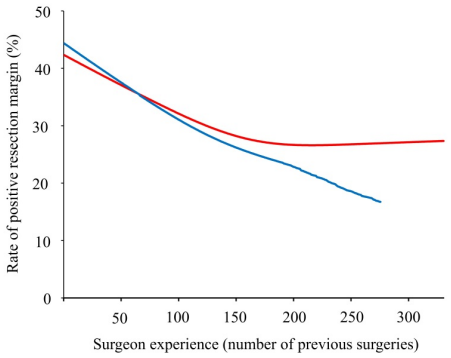

Figure 2: Learning curve for obtaining a negative resection margin. Red: all surgeons, blue: single surgeon (KH).

The learning curve for obtaining a negative resection margin is shown in Figure 2. In the case of all surgeons, whenever the number of surgical cases increases, the PRM decreases, and the learning curve plateaus after 167 cases. In this point, the rate of PRM was 27.4%. However, the learning curve of single surgeon (KH) did not plateau after 250 cases. The rate of his last PRM was 16.7%.

Discussion

Radical prostatectomy is now performed by robot-assisted radical prostatectomy (RARP). Since the long-term results of LRP have been reported, it is important to discuss the outcome with RARP [7-10,13]. Soares et al reported the results of LRP in 1,138 patients who were studied from 2000 through 2008 [10]. They found that the 5-year PSA failure-free rate was 85.4% for a median observation period of 88.6 months. In our study, the 5-year PSA failure-free rate was 70.5%, and the prognostic factors for PSA failure were resection margin, EPE, and tumor diameter. The 5-year PSA failure-free survival for patients with a negative resection margin was 81.6%, and these results were similar to that in other reports [7-10,13].

Many investigators reported prognostic factors for PSA failure, such as resection margin, PSA level, and pathological stage [7-10]. Among these prognostic factors, resection margin status was important because the PRM rate could be reduced by improvement of the surgical technique. Sooriakumaran et al. reported that among 22,393 cases, the PRM of LRP was 16.3%, and that it was better than that of RRP, but was worse than that of RARP [14]. Other reports, including many LRP cases, concluded that the PRM varied from 7.4% to 29.2% [7-10]. Yossepowitch et al. reported that a PRM increased the PSA failure rate 1.6-5.0-fold [15]. In our study, the PRM rate was 30.5% in all case, and 27.7% in the pT2 patients and 39.0% in the pT3 patients, and these results were the same as previous reports [7-10]. The factors associated with a PRM were tumor location, nerve sparing procedure, and tumor diameter. Some studies found that a PRM was associated with nerve sparing and a high-volume center, but the tumor location was not evaluated [14,16].

In our study, the tumor was more common in the apex, and a PRM was highest in the apex. Indeed, the apex anterior location is important. In Japan, it was previously reported that most common tumor location was in the apex [17]. In our study, the tumor location was almost equally distributed between apex-anterior and posterior, but the PRM frequency was higher in the anterior. The surgical technique for an apical dissection is difficult because the apex-anterior is absence of the prostatic capsule. Wide resection of the apex may reduce PRM resulting in a good oncological outcome but this procedure causes incontinence. Both an understanding of precise dissection and surgical experience are important to reduce the rate of PRM. The tumor location was associated with the PRM but it was not associated with PSA failure. In other words, the PSA failure-free survival was improved by having negative resection margin even regardless of where the tumor was located. On the other hand, it was reported that apex-cancer had favorable outcome, and further observation is necessary [18,19].

It was reported that PRM was decreased in high-volume surgical centers when compared to that in low-volume centers. The learning curve generally needed 200-250 cases for the optimal resection margin results [20,21]. Secin et al. reported that the rate of decrease in PRM was more slowly for LRP than for RRP [20]. Additionally, Vickers et al. reported that PSA failure decreased to 16% after 250 patients and to 9% after 750 patients [21]. LRP may be more difficult to learn because LRP must be operated in a two-dimensional space without a direct view of surgical space, with longer instrument and diminished haptic feedback. RRP is a relatively mature procedure, on the other hand, LRP is a recently developed surgical technique. Therefore improvement of the surgical technique in LRP was always considered. Because of these reasons, the learning curve is longer in comparison with that of RRP. After having reached the plateau once, the rate of PRM decreases according to experience of surgical cases [20,21]. Our finding in this study was same as these reports. Because the learning curve for LRP is long, teaching program is important. Surgeons need to understand how PRM occurred by reviewing intraoperative video recording with pathological findings and make an effort for technical improvement. In this study, one surgeon could reduce the PRM until 16%. He is acquainted with dissection and removes the apex as widely as possible, but he is careful to leave the urethra as long as possible.

LRP has been discussed in comparison with RRP, but recently LRP has been compared with RARP [13,22]. The oncological outcome was same in many reports, including the two past randomized control trials (RCTs) [23,24]. These RCTs compared LRP with RARP and reported that PRM was 10.0 to 20.0% in LRP and 15.4 to 26.6% on RARP. Surgeons in these RCTs performed over 600 LRP. According to learning curve for PRM, it was reported that RARP is earlier than other surgical procedure, but there were some reports that the learning curve needed 200-250 cases for the optimal resection margin results [25,26]. In addition, the other RCT comparing RARP and RRP have been published recently [27]. This report shows that the PRM was the same in both groups. Based on these RCTs, oncological outcome of RARP was shown as same as RRP and LRP, and RARP spread out worldwide from good operability.

There were some limitations in our study. This cohort was small and the follow-up period was relatively short. The observation period in this study was 48.1 months and longer follow-up period is needed for assessing prognostic factors. To discuss the treatment outcome, CSS was more important than PSA failure-free survival. According to PSA failure, this observation period was not enough but pathological and surgical outcome were enough to evaluate and provide important and informative results. The surgical method of radical prostatectomy is now changing to RARP in many institutions. However, based on the results in this LRP study, it will be possible to improve the surgical technique in the future.

References

1. Schuessler WW, Schulam PG, Clayman RV, Kavoussi LR (1997) Laparoscopic radical prostatectomy: initial short-term experience. Urology 50: 854-857.
2. Raboy A, Ferzli G, Albert P (1997) Initial experience with extraperitoneal endoscopic radical retropubic prostatectomy. Urology 50: 849-853.
3. Guillonneau B, Cathelineau X, Barret E, Rozet F, Vallancien G (1999) Laparoscopic radical prostatectomy: technical and early oncological assessment of 40 operations. Eur Urol 36: 14-20.
4. Jacobsen NE, Moore KN, Estey E, Voaklander D (2007) Open versus laparoscopic radical prostatectomy: a prospective comparison of postoperative urinary incontinence rates. J Urol 177: 615-619.
5. Matsuda T, Ono Y, Terachi T, Naito S, Baba S, et al. (2006) The endoscopic surgical skill qualification system in urological laparoscopy: a novel system in Japan. J Urol 176: 2168-2172.
6. Tanaka M, Ono Y, Matsuda T, Terachi T, Suzuki K, et al. (2009) Guidelines for urological laparoscopic surgery. Int J Urol 16: 115-125.
7. Hruza M, Bermejo JL, Flinspach B, Schulze M, Teber D, et al. (2013) Long-term oncological outcomes after laparoscopic radical prostatectomy. BJU Int 111: 271-280.
8. Busch J, Stephan C, Herold A, Erber B, Kempkensteffen C, et al. (2012) Long-term oncological and continence outcomes after laparoscopic radical prostatectomy: a single-centre experience. BJU Int 110: E985-990.
9. Verze P, Scuzzarella S, Martina GR, Giummelli P, Cantoni F, et al. (2013) Long-term oncological and functional results of extraperitoneal laparoscopic radical prostatectomy: one surgical team's experience on 1,600 consecutive cases. World J Urol 31: 529-534.
10. Soares R, Di Benedetto A, Dovey Z, Bott S, McGregor RG, et al. (2015) Minimum 5-year follow-up of 1138 consecutive laparoscopic radical prostatectomies. BJU Int 115: 546-553.
11. Hashine K, Ueno Y, Shinomori K, Ninomiya I, Teramoto N, et al. (2012) Correlation between cancer location and oncological outcome after radical prostatectomy. Int J Urol 19: 855-860.
12. Hashine K, Nakashima T, Iio H, Ueno Y, Shimizu S, et al. (2014) Health-related quality of life in the first year after laparoscopic radical prostatectomy compared with open radical prostatectomy. Jpn J Clin Oncol 44: 686-691.
13. Novara G, Ficarra V, Mocellin S, Ahlering TE, Carroll PR, et al. (2012) Systematic review and meta-analysis of studies reporting oncologic outcome after robot-assisted radical prostatectomy. Eur Urol 62: 382-404.
14. Sooriakumaran P, Srivastava A, Shariat SF, Stricker PD, Ahlering T, et al. (2014) A Multinational, Multi-institutional Study Comparing Positive Surgical Margin Rates Among 22393 Open, Laparoscopic, and Robot-assisted Radical Prostatectomy Patients. Eur Urol 66: 450-456.
15. Yossepowitch O, Briganti A, Eastham JA, Epstein J, Graefen M, et al. (2014) Positive surgical margins after radical prostatectomy: a systematic review and contemporary update. Eur Urol 65: 303-313.
16. Ou YC, Yang CK, Chang KS, Wang J, Hung SW, et al. (2014) The surgical learning curve for robotic-assisted laparoscopic radical prostatectomy: experience of a single surgeon with 500 cases in Taiwan, China. Asian J Androl 16: 728-734.
17. Takashima R, Egawa S, Kuwao S, Baba S (2002) Anterior distribution of Stage T1c nonpalpable tumors in radical prostatectomy specimens. Urology 59: 692-697.
18. Kim M, Choi SK, Park M, Shim M, Song C, et al. (2016) Characteristics of Anteriorly Located Prostate Cancer and the Usefulness of Multiparametric Magnetic Resonance Imaging for Diagnosis. J Urol 196: 367-373.

19. Wadhwa H, Terris MK, Aronson WJ, Kane CJ, Amling CL, et al. (2016) Long-term oncological outcomes of apical positive surgical margins at radical prostatectomy in the Shared Equal Access Regional Cancer Hospital cohort. Prostate Cancer Prostatic Dis 19: 423-428.
20. Secin FP, Savage C, Abbou C, de La Taille A, Salomon L, et al. (2010) The learning curve for laparoscopic radical prostatectomy: an international multicenter study. Int Braz J Urol 184: 2291-2296.
21. Vickers AJ, Savage CJ, Hruza M, Tuerk I, Koenig P, et al. (2009) The surgical learning curve for laparoscopic radical prostatectomy: a retrospective cohort study. Lancet Oncol 10: 475-480.
22. Moran PS, O'Neill M, Teljeur C, Flattery M, Murphy LA, et al. (2013) Robot-assisted radical prostatectomy compared with open and laparoscopic approaches: a systematic review and meta-analysis. Int J Urol 20: 312-321.
23. Asimakopoulos AD, Pereira Fraga CT, Annino F, Pasqualetti P, Calado AA, et al. (2011) Randomized comparison between laparoscopic and robot-assisted nerve-sparing radical prostatectomy. J Sex Med 8: 1503-1512.
24. Porpiglia F, Morra I, Lucci Chiarissi M, Manfredi M (2013) Randomized controlled trial comparing laparoscopic and robot-assisted radical prostatectomy. Eur Urol 63: 606-614.
25. Abboudi H, Khan MS, Guru KA, Froghi S, de Win G, et al. (2014) Learning curves for urological procedures: a systematic review. BJU Int 114: 617-629.
26. Thompson JE, Egger S, Bohm M, Haynes AM, Matthews J, et al. (2014) Superior quality of life and improved surgical margins are achievable with robotic radical prostatectomy after a long learning curve: a prospective single-surgeon study of 1552 consecutive cases. Eur Urol 65: 521-531.
27. Yaxley JW, Coughlin GD, Chambers SK, Occhipinti S, Samaratunga H, et al. (2016) Robot-assisted laparoscopic prostatectomy versus open radical retropubic prostatectomy: early outcomes from a randomised controlled phase 3 study. Lancet 388: 1057-1066.