นิพนธ์ต้นฉบับ

Incidence of Urinary Incontinence and Erectile Dysfunction Post Robotic-Assisted Laparoscopic Radical Prostatectomy : The First 318 Cases in Siriraj Hospital, Thailand.

Chainarong Nithisathian, Chaiyong Nualyong, Sunai Leewansangtong, Sittiporn Srinualnad, Tawatchai Taweemonkongsap, Bansithi Chaiyaprasithi, Teerapon Amornvesukit, Kittipong Phinthusophon, Siros Jitpraphai, Patkawat Ramart, Phichaya Sujijantararat, Suchai Soontrapa

Abstract

Objective: To evaluate the incidence of urinary incontinence and erectile dysfunction (ED) at 12 month post robotic-assisted laparoscopic radical prostatectomy (RALP) in Siriraj hospital. To evaluate the risk factor (age, pre-operative PSA, Gleason score, T-staging, Margin, status post-operative PSA, Nerve sparing, Case number) for incontinence and ED at 12 months post RALP in Siriraj hospital

Materials and Methods: Between February 2007 to December 2009, the continence and erectile function of 318 patients that underwent RALP were evaluated by questionnaire-base research design. Incontinence was defined as the use of more than one safety pad per day. Erectile function was assessed by IIEF-5 scores which less than 22 was dysfunction. Direct questions of the ability to have erection and ability to have sexual intercourse were also used to assess erectile function.

Results: The rate of urinary incontinence post RALP at 1 year was 26.7%. The rate of erectile dysfunction post RALP at 1 year was 92.5% (294) in total. In bilateral nerve sparing group (N=107), 16.8% achieved IIEF-5 scores ≥22, 76.2% were able to have erection and 57.4% were able to have erection sufficient for

Division of Urology, Department of Surgery, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand

intercourse. When adjuvant hormonal therapy was excluded from patients in bilateral nerve sparing group, 80.2% were able to have erection and 62.9% were able to have erection sufficient for intercourse. The significant risk factor for incontinence post RALP was non-nerve sparing. For erectile function post RALP, the significant factors were age, pre-operative PSA, T-staging, nerve sparing and surgical experience (Case number).

Conclusion: The rate of incontinence post RALP in this study was acceptable. However the rate of ED post RALP was higher than in previous studies which could be due to lacking of pre-operative IIEF-5 scores and adjuvant androgen deprivation therapy (35.5% of the patients). A more appropriate tool for evaluation is needed for further evaluation.

Keywords: Robotic-assisted, Laparoscopic, Radical prostatectomy, RALP, continence, erectile dysfunction

Prostate cancer is the most frequently diagnosed noncutaneous cancer in American men and the second leading cause of cancer death. Although several options are available to the patient, surgical cure continues to be a mainstay of therapy.[1]

A century has passed since Hugh Hampton Young performed the first open prostatectomy for carcinoma through a perineal approach. In 1947, Millin reported on the retropubic approach to prostatectomy. Although effective as a technique for curing prostate cancer, radical retropubic prostatectomy (RRP) was fraught with significant morbidity, including excessive blood loss, urinary incontinence, and impotence. In the late 1970 and early 1980 several detailed anatomic studies performed in fetal and adult cadavers provided important insights into the periprostatic anatomy, especially that of the dorsal venous complex, neurovascular bundle, and striated urethral sphincter. These landmark observations led to an anatomic approach to radical prostatectomy and, more importantly, a significant reduction in operative morbidity. As a result, the anatomic nerve-sparing radical retropubic prostatectomy has remained the cornerstone of surgical treatment for clinically localized prostate cancer.[2]

In an effort to further decrease the morbidity of open prostatectomy, a minimally invasive surgical approach to treating prostate cancer was described by Schuessler and colleagues in 1997, who performed the first successful laparoscopic radical prostatectomy (LRP). Based on a series of 9 patients, The recent introduction of advanced robotic devices such as the daVinci Surgical System (Intuitive Surgical, Inc., Sunnyvale, CA) to the field of urologic surgery has added new hopes of reducing operative times and the learning curve for minimally invasive prostatectomy. By incorporating sophisticated wristed technology at the terminal ends of the robotic instruments, a surgeon is able to operate, suture, and dissect with the facility of a human wrist. In addition, the superior three-dimensional view offered by this robotic system provides the surgeon with an unprecedented view of the periprostatic anatomy.[2]

Since the first robotic-assisted laparoscopic radical prostatectomy (RALP) was performed on 16 Feb 2007 in Siriraj hospital, over 500 prostate cancers have been treated with this procedure thereafter. However, the questions about risk, benefit, and cost-effectiveness were concerned.

According to the previous studies Vincenzo Ficarra et al, have found that incontinence rates at 12 month follow-up for RALP was 2-16% and ED is about 3-80% at 12 month follow-up for nerve-sparing RALP[3,4]. Coelho et al, have found that the weighted mean continence rates at 12 month follow-up for Retropubic radical prostatectomy (RRP), Laparoscopic radical prostatectomy (LRP), and RALP was 79%, 84.8% and 92%, respectively. The weighted mean potency rates for patients who underwent unilateral or bilateral nerve sparing at 12 month follow-up were 43.1% and 60.6% for RRP, 31.1% and 54% for LRP, and 59.9% and 93.5% for RALP[5]. Furthermore, Tewari et al showed that the median time to continence was significantly shorter after RALP comparing to RRP[6]. This beneficial evidence was also confirmed by Joseph et al, who showed continence at 6 month 92% from LRP and 90% from RALP in his study[7].

For erectile dysfunction following the three procedures (RALP, LRP and RRP), Anastasiadis et al, Roumeguere et al, and Touijer et al have showed no statistically significant between RRP and LRP [8,9,10,11] but Tewari et al have found that the return of erection was shorter for RALP (180 days) compared with RRP (440 days)[6].

Though the above international studies show the benefit of RALP over LRP and RRP in term of continence and erectile function, there is still yet data about this in Thai population. This study is to defy the incidence and risk factors of incontinence and erectile dysfunction (ED) in patient who underwent RALP for prostate cancer in Siriraj hospital.

Materials and Methods

Patients

Between February 2007 to December 2009, 479 patients underwent RALP at Siriraj hospital, Bangkok, Thailand. 456 Patients were included due to adequacy of contact data. Demographic data, pre-operative, intra-operative and post-operative data were reviewed from OPD and IPD documents. 456 patients were contacted by mail then by phone as necessary. Pad test and IIEF-5 questionnaires were used as the tool in this study.

318 (71.19%) patients were included in this study and 138 (28.81%) patients were excluded due to unable to contact the patients, conversion to open surgery, patients had passed away and the patients or relatives denied to participate in the study. 180 patients replied by mail and 138 patients required additional contact by phone Nerve sparing and non-nerve sparing data were documented in 220 patients.

Surgery

All 318 RALP were performed by six surgeons. The nerve sparing was performed in case of low risk of extracapsular invasion and being potent preo-peratively. Main technical points are to identify pre-existing anatomic planes and to avoid of thermal injury near the nerves.

Pathological analysis

Prostate and pelvic lymph node specimens were examined by pathologists. A positive surgical margin was defined by the pathologist as extension of the tumor to the inked surface of the specimen.

Oncological outcome

Pathologic stage according to the 2002 TNM classification, Gleason score, and margin status were routinely recorded. Post-operative PSA categorized as PSA level of >0.4 ng/ml and below at 2 month after operation. Pathological risk factor were categorized according to D'Amico risk classification (Pre-operative PSA, T staging, Gleason score)

Functional outcome

Sexual and urinary function were assessed by questionnaire (Pad test, IIEF-5 and direct questions of the ability to have erection and sexual intercourse) by mail and by phone. Continence was defined as the use of less or equal to one safety pad a day. Those who used more than one safety pad a day were categorized as incontinent. Erectile function was assessed by IIEF-5 scores and direct questions of the ability to have erection and sexual intercourse. A patient was considered potent if his score more than or equal to 22 with or without any therapy.

Data

All data were collected on data sheets, transferred to a database and analyzed with SPSS. Incidence data are presented as frequency. The potential risk factors were analyzed by Chi-square. A P-value of less than 0.05 was considered significant.

Results

318 patients underwent RALP in Siriraj hospital. The characteristics of the patients are shown in Table 1. Most of the patients were older than 60 years old. Overall negative surgical margin rate was 52.2% and most of the post-operative PSA were below 0.4 ng/mL.

The incidence of urinary incontinence is shown in Table 2 and the incidences of ED are shown in Table 3. The incidence of urinary incontinence after 12 months of surgery is 73.3%. The incidences of erectile dysfunction are shown in Table 3 and are categorized by nerve-sparing status. The ED according to IIEF-5 is 92.5%. The incidence of possible to have erection in bilateral nerve sparing without adjuvant ADT group is 80.2% and the incidence of not able to have sexual intercourse in non-nerve sparing group is 81.6%.

The different outcomes between the first 200 cases and after are shown in Table 4. The incidence of possible to have erection in bilateral nerve sparing without ADT group improved from 75.9 to 82.7%. The surgical experience factor is statistically significant to erectile function outcome in the case number after 200 with the p value <0.05.

The significant factors to urinary incontinence and erectile function are shown in Table 5 which reveal nerve sparing is the related factor to continence outcome (P<0.05). Furthermore, the age, pre-operative PSA, T-staging, nerve sparing and surgical experience are the related factors to erectile function post RALP.

Discussion

Since the first prostatectomy by Hugh Hampton Young many surgical techniques have been changed, but the concerning in treatment of the oncological and the functional outcome were maintained.

Since the first RALP in Siriraj hospital, the data of 318 patients were collected for analysis. The incidence of incontinence after 12 months post-operation is 26.7%. Multiple factors were analyzed to identify the related factors. The patient age, pre-operative PSA, Gleason score, T-staging, margin status, post-operative PSA, nerve-sparing and case numbers were analyzed. Nerve-sparing is the only significant factor in this study. The outcome of this study is supported by the finding of Matthew M Lux, et al. which identify nerve-sparing as the protective factor for incontinence[12] and the finding of Louis S Krane, et al. showed that pre-operative BMI, SHIM, IPSS, prostatic weight, age, posterior stitch no individual demographic are associated with urinary continence post RALP[13]. The incidence of incontinence post RALP in this study is higher from the previous literature, which could be due to the rate of nerve sparing was only 60.45%.

Table 1 *Demographic data*

	Mean ± SD (Min-Max) % (N)	N
Age (years)	66.64±7.795 (40-84)	318
<60	20.4 (65)	
≥60	79.6 (253)	
Pre-operative PSA (ng/ml)	18.10±28.65 (0.3-300)	318
<10	48.7 (155)	
10-20	31.1 (99)	
>20	20.1 (64)	
Gleason score	7.10±0.93 (4-9)	316*
≤6	23.4 (74)	
7	53.2 (168)	
≥8	23.4 (74)	
T-Staging		318
T0-T2a	19.8 (63)	
T2b-T2c	44.7 (142)	
T3a or higher	35.5 (113)	
Margin		318
Free margin	52.2 (166)	
Positive margin	47.8 (152)	
Post-operative PSA after 2 month (ng/ml)	0.24±2.64 (0.00-45.37)	301**
<0.4	93.7 (282)	
≥0.4	6.3 (19)	
Nerve sparing		220***
Non-nerve sparing	39.5 (87)	
Unilateral nerve sparing	11.8 (26)	
Bilateral nerve sparing	48.6 (107)	
Case Number	237.22±130.98 (1-456)	
1-200	40.9 (130)	
201-456	59.1 (188)	

* data loss due to incomplete pre-operative data record and pathological report pT0 post operative

** data loss due to patient loss follow up at Siriraj hospital

*** data loss due to incomplete data record

Table 2 *Outcome of urinary incontinence*

	% (N)
Pad test	
≤ One safety pad a day	73.3 (233)
> One safety pad a day	26.7 (85)

Table 3 *Erectile function according to type of nerve sparing and adjuvant hormonal treatment.*

		IIEF-5 (22-25)		Erection		Able to intercourse	
Type	**N = 212**	**%**	**(N)**	**%**	**(N)**	**%**	**(N)**
Non-nerve sparing	87	1.1	(1)	32.1	(28)	18.4	(16)
Unilateral nerve sparing (All)*	24	8.3	(2)	62.5	(15)	37.5	(9)
Unilateral nerve sparing without ADT*	13	15.4	(2)	61.5	(8)	38.5	(5)
Bilateral nerve sparing (All)*	10	117.8	(18)	76.2	(77)	57.4	(58)
Bilateral nerve sparing without ADT*	81	20.9	(17)	80.2	(65)	62.9	(51)

* 6 cases from bilateral nerve sparing group and 2 cases from unilateral nerve sparing group. ADT data loss due to incomplete data record and loss follow up at Siriraj hospital.

Table 4 *Erectile function in nerve sparing according to learning curve.*

		IIEF-5 (22-25)		Erection		Able to intercourse	
Type	**N = 125**	**%**	**(N)**	**%**	**(N)**	**%**	**(N)**
Unilateral nerve sparing (All)*							
(1-200)	16	-	(0)	56.3	(9)	25	(4)
(201-456)	8	-	(0)	75	(6)	62.5	(5)
Unilateral nerve sparing without ADT*							
(1-200)	7	14.3	(1)	57.1	(4)	28.6	(2)
(201-456)	6	16.7	(1)	66.7	(4)	50	(3)
Bilateral nerve sparing (All)*							
(1-200)	39	-	(0)	74.4	(29)	48.7	(19)
(201-456)	62	1.6	(1)	77.4	(48)	62.9	(39)
Bilateral nerve sparing without ADT*							
(1-200)	29	10.3	(3)	75.9	(22)	55.1	(16)
(201-456)	5226.9	(14)	82.7	(43)		67.3	(35)

* 6 cases from bilateral nerve sparing group and 2 cases from unilateral nerve sparing group. ADT data loss due to incomplete data record and loss follow up at Siriraj hospital.

Table 5 *Factors related to urinary incontinence and erectile dysfunction*

Factors	**Incontinence (P-value)**	**ED (P-value)**
Age	0.135	0.006
Pre-operative PSA	0.057	0.018
Gleason score	0.442	0.095
T-staging	0.119	0.011
Margin	0.199	1.000
Post-operative PSA after 2 month	0.733	0.614
Nerve-sparing (Unilateral and Bilateral)	0.005	0.001
Number of cases (after 200 cases)	0.521	0.038

The incidence of presence of erection after 12 months post RALP in this study is 80.2%. Multiple factors were analyzed to find the correlation with the incidence of erectile dysfunction. Age, pre-operative PSA, T-staging, nerve sparing and surgical experience are all the correlated factors with erectile dysfunction. Age, coronary artery disease, diabetes mellitus, quality of pre-operative erection, frequency of intercourse, hypertension, neurovascular bundle preservation and the use of PDE-5 inhibitor preoperatively predicted the preservation of potency according to the finding of Tracy Marien[14,15]. Menon also showed significantly higher 3- and 6-mo potency rates in patients younger than 60 years, compared to older patients operated on with the same surgical technique[16]. Three more factors are considered to be correlated to post-operative erectile dysfunction (pre-operative PSA, T-staging and surgical experience).

According to the demographic data, most of patients were older than 60 years and also the majority is in the stage higher than T2a. These could explain the incidence of erectile dysfunction in this study. Furthermore, the lack of pre-operative IIEF-5 data could be a problem to exclude the pre-operative erectile dysfunction patients. In fact IIEF-5 is a strong questionnaire with a score above 22 points required to classify as good erectile function. The intermediate erectile function was classified as erectile dysfunction by this questionnaire.

Conclusion

The incidence of incontinence for early experience of RALP in Siriraj hospital is 26.7% and the correlated factor is non-nerve sparing. The incidence of ability to have erection post bilateral nerve sparing RALP without ADT is 80.2% and the correlated factors are age, pre-operative PSA, T-staging, nerve sparing and surgical experience.

Further studies are required because the lack of pre-operative IIEF-5 for control and the more appropriate questionnaire tool to assess the erectile function.

References

1. David M. Hartke, MD, Martin I. Resnick, MD; Radical perineal prostatectomy. In: Wein AJ, Kavoussi LR, Novick AC, Partin AW, Peters CA ed. Campbell-Walsh Urology 9th ed. Philadelphia, **Saunder** 2006: p.2979.
2. Li-Ming Su, Joseph A., Smith Jr. Laparoscopic and Robotic-Assisted Laparoscopic Radical Prostatectomy and Pelvic Lymphadenectomy. In: Wein AJ, Kavoussi LR, Novick AC, Partin AW, Peters CA ed. Campbell-Walsh Urology 9th ed. Philadelphia, **Saunder** 2006: p.2985-6.
3. Ficarra V, Novara G, Artibani W, Cestari A, Galfano A, Graefen M, et al. Retropubic, Laparoscopic, and Robot-Assisted Radical Prostatectomy: A Systemic Review and Cumulative Analysis of Comparative Studies. **Eur Urol** 2009; 55:1037-63
4. Ficarra V, Cavalleri S, Novara G, Aragona M, Artibani W. Evidence from Robo-Assisted Laparoscopic Radical Prostatectomy: A systematic review. **Eur Urol** 2007; 51:45-56.
5. Coelho RF, Rocco B, Patel MB, Orvieto MA, Chauhan S, Ficarra V, Melegari S, et al. Retropubic, Laparoscopic, and Robo-Assisted Radical Prostatectomy: **A Critical Review of Outcomes Reported by High-Volume Centers J Endourol** 2010; 24.
6. Tewari A, Srivasatava A, Menon M. Members of the VIP team. A prospective comparison of radical retropubic and robot-assisted prostatectomy: experience in one institution. **BJU Int** 2003; 92:205-10.
7. Joseph JV, Vicente I, Madeb R, Erturk E, Patel HR. Robot-assisted versus pure laparoscopic radical prostatectomy: are there any differences? **BJU Int** 2005; 96:39-42.

8. Anastasiadis AG, Salomon L, Katz R, Hoznek A, Chopin D, Abbou CC. Radical retropubic versus laparoscopic prostatectomy: a prospective comparison of functional outcome. **Urology** 2003; 62:292-7.

9. Roumeguere T, Bollens R, Vanden Bossche M, Rochet D, Bialek D, Hoffman PM, et al. Radical prostatectomy: a prospective comparison of oncological and functional results between open and laparoscopic approaches. **World J Urol** 2003; 20:360-6.

10. Touijer K, Eastham JA, Secin FP, Romero Otero J, Serio A, Stasi J, et al. Comprehensive prospective comparative analysis of outcomes between open and laparoscopic radical prostatectomy conducted in 2003 to 2005. **J Urol** 2008; 179:1811-7.

11. Rozet F, Harmon J, Cathelineau S, Barret E, Vallancien G. Robot-assisted versus pure laparoscopic radical prostatectomy. **World J Urol** 2006; 24:171-9.

12. Matthew M Lux, Tricia D Greene, Changyong Feng, Erdal Erturk, Hitendra R Patel, Jean V Joseph. Does nerve sparing contribute to continence in patients with poor preoperative erectile function? **J Urol** 2009; 181(4) supplement: 679-84.

13. Krane LS, Bhandari AM, Stricker HJ. Posterior urethrovesical stitch does not improve early continence in men undergoing robotic radical prostatectomy. **J Urol** 2009; 181(4) supplement: 679-84.

14. Marien T, Sankin A, Lepor H. Factors Predicting Preservation of Erectile Function in Men Undergoing Open Radical Retropubic Prostatectomy. **J Urol** 2009; 181:1817-22.

15. Esequiel Rodriguez, Jr., David S. Finley, Douglas Skarecky andThomas E. Ahlering. Single Institution 2-Year Patient Reported Validated Sexual Function Outcomes After Nerve Sparing Robot Assisted Radical Prostatectomy. **J Urol** 2009; 181:259-63

16. Menon M, Tewari A, Vattikuti Institute Prostatectomy Team. Robotic radical prostatectomy and the Vattikuti Urology Institute technique: an interim analysis of results and technical points. **Urology** 2003; 61:15-20