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Radical prostatectomy after vascular-targeted photodynamic therapy (VTP) with TOOKAD® : feasibility, early and intermediate results.

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Keywords: Radical prostatectomy, Focal therapy, Vascular-targeted photodynamic therapy, salvage prostatectomy, functional outcomes

The aim of our study is to evaluate, the feasibility and results of prostatectomy after targeted vascularization photodynamic therapy. It was feasible and safe. Despite minor difficulties oncological and functional outcomes were similar to regular radical prostatectomies.

ABSTRACT

Introduction and objectives: vascular-targeted photodynamic therapy with TOOKAD® (VTP) is a new therapeutic option for localized prostate cancer (PCa) management. The objectives are to assess the feasibility of radical prostatectomy (RP) after VTP and describe functional and oncological outcomes.

Material and Methods : we retrospectively included 45 patients who underwent salvage RP after VTP for recurrent PCa in 14 surgical centres in Europe between October 2008 and March 2017.Forty-two RP were performed: 16 robot-assisted, 6 by laparoscopy, and 20 by open surgery. Primary endpoints were morbidity and technical difficulties. Secondary endpoints were early and intermediate post-operative functional and oncologic outcomes.

Results: Median operative time was 180 (150-223) minutes. Median blood loss was 200 (155-363) millilitres. According to the surgeons, the surgery was “easy” for 29 patients (69%), “difficult” for 13 patients (31%). Nerve sparing was feasible for 14 patients (33%). Five (12%) post-operative complications were found: 2 Claviens I, 2 Clavien II and 1 Clavien IIIB. There was 13 pT3 (31%), 21 (50%) pT2c. Surgical margins were positive for 13 patients (31%). PSA was undetectable at 6-12 months for 37 patients (88%). Nine patients had complementary radiotherapy. Four patients had a last PSA > 0.2 ng/mL with a median follow-up of 23 (12-36) months. At one year, 27 patients (64%) were completely continent (no pads), 10 (24%) had low incontinence (1 pads). Four patients (11 %) recovered potency without treatment, and 23 (64%) with appropriate treatment.

Conclusion: Salvage RP after VTP treatment was feasible and safe without difficulties for most of the surgeons.

INTRODUCTION:

Prostate cancer (PCa) is the most common neoplasm in men [1]. Mortality due to PCa has declined since the 1990s as a consequence to individual screening and early treatment [2].

The current treatment strategies for localized PCa are either active surveillance (AS) or radical therapies such as radical prostatectomy (RP). On one hand, AS might present a risk of progression [3] and on the other hand, radical therapies induce significant morbidity with negative impact on quality of life [4] .

Vascular-targeted photodynamic TOOKAD therapy (VTP) allows focal ablation resulting from rapid occlusion of tumour vascularization within a few minutes of treatment. This treatment was well tolerated in a randomized study comparing VTP to AS[5]. VTP appears therefore to be an alternative for patients who wish to be treated with limited risk of side effects [5,6].

Despite studies showing a short-term effectiveness of focal treatments in selected patients and tumours [5,6], the use of focal therapy needs to be thoroughly studied [7,8]. A major question is to assess the impact of focal therapies on the subsequent therapeutic options in case of failure [9,10]. Therefore, the aim of this study was to assess the feasibility, the safety and the efficacy of salvage RP for recurrent PCa after TOOKAD® VTP.

MATERIAL AND METHODS:

Study design

This was a retrospective study that included all patients who underwent salvage RP after VTP for recurrent PCa in 14 surgical centres in Europe between October 2008 and March 2017. These patients were initially included in one of the two phase II non-randomised studies, PCM201 and PCM203, or in the phase III European randomised study PCM301.

Data collection

For each patient, the following data was prospectively extracted: age at the time of VTP, pre-VTP biopsy data. Control biopsies were systematically performed at 6 months for patients included in the phase II studies, at 12 and 24 months for patients in the phase III. Subsequent biopsies were performed if there was either a PSA progression confirmed by 2 successive tests or a clinical progression on digital rectal examination. Progression was defined as a shift from the low-risk to the intermediate or high-risk prognosis groups according to the d'Amico classification. We used the contemporary 2015 PCa grading system (International Society of Urological Pathology (ISUP) group 1: Gleason 3+3, group 2: 3+4, group 3: 4+3, group 4: Gleason 8, group 5: Gleason 9 or 10) [11]. We also recorded whether a second procedure of VTP was performed prior to prostatectomy.

The following data was collected retrospectively: time between VTP and prostatectomy, operative data (blood loss, transfusion, operating time, conversion, observed surgical difficulties, extent of nerve sparing (NS)), perioperative outcomes (including urethral catheterisation time, hospital stay, and post-operative complications). Complications were graded according to the Dindo-Clavien classification (5).

Surgical difficulties were classified as "easy" or "difficult". The nature of the surgical difficulties and per-operative complications was described retrospectively.

Short-term oncological outcomes were assessed by pathological analysis of the whole mount specimen. Mid-term oncological outcomes were assessed by Prostatic Specific Antigen (PSA) measurements and subsequent additional oncologic treatment. Biochemical recurrence was defined as PSA > 0.2 ng/ml measured twice successively [1].

"Complete continence" was defined as the absence of need for pads., "low continence" as effort leakage with the need for 1 pad/day, "medium continence" as the need for 2 pads/day and "complete incontinence" as permanent urinary leakage with the need for >2 pads/day. Erectile function was described as following: possibility of sexual intercourse without treatment, with treatment or no possibility of sexual intercourse.

Statistical analysis

Quantitative variables were described by their median and interquartile range and compared between groups by Wilcoxon tests. Qualitative variables were described by their frequencies and percentages and compared by Fisher's exact tests. A p value less than 0.05 was considered significant.

Statistical analysis was made with the software R, version 3.1.0.

RESULTS:

We analysed the files of 313 patients who had a VTP procedure during one of the two phase II non-randomised studies, PCM201 and PCM203, or in the phase III European randomised study PCM301.

Of all the patients treated with VTP, 45 patients underwent subsequent RP (19%) for recurrent PCa after VTP. Three patients were excluded because of insufficient data. Data from 42 patients were analyzed with a median post-prostatectomy follow-up of 23 (12-36) months.

Patient's characteristics before VTP and prostatectomy are reported in Table 1.

Median age at the time of RP was 65 years (IQR: 61-67). Median prostatic volume before VTP was 35 mL (30-46). Median PSA before RP was 5.9 (3.2-7.9) ng/mL.

Median time between VTP and prostatectomy was 17 months (12-36). Five patients (12%) had a second VTP-procedure. Among the 42 prostatectomies, 16 were robot-assisted, 6 by laparoscopy, and 20 by open surgery. No conversion was necessary during laparoscopic or robot-assisted surgery.

Peri-operative outcomes are reported in Table 2. Median operating time was 180 (150-223) minutes. Median blood loss was 200 (155-363) mL.

According to the postoperative report, the surgery was considered "easy" for 29 patients (69%), "difficult" for 13 patients (31%). In most cases, the reported difficulty was due to lateral fibrosis during the dissection of thee nerve bundles on the VTP treated-lobe; the other difficulty was linked to posterior fibrosis with adherence to the rectum, leading in two cases significant difficulties to separate the rectum from the posterior face of the Denonviliers fascia. There were no rectal injuries reported during the procedures or postoperatively. There were no rectal injuries. Bilateral NS was feasible for 10 patients (24%) and unilateral NS for 4 patients (10%). There was no NS in 28 cases (67%). Most surgeons reported that, NS on the non-treated side was not more difficult than usual. On the treated side, preservation was careful and the use of the bipolar forceps instead of clips because of tissue adherences was more often needed. Usually the surgeons began by the non-treated lobe, which was considered easier.

Median urethral catheterization was 7 (7-8) days. Median hospital stay was 7 (5-8) days. No peri-operative mortality was reported. Five (12%) post-operative complications were found: 2 Claviens I (transient ileus, one wound infection), 2 Clavien II (febrile urinary tract infection) and 1 Clavien IIB (an accidental ureteral section occurred during the pelvic lymphadenectomy of an open-prostatectomy and required a direct reanastomosis and 18 days of urethral catheterization).

Oncological outcomes are reported in Table 3. Surgical margins were positive for 13 patients (31%), 7 on the treated side (54%). Only one of the 14 patients who had NS had positive surgical margins

(PSM) (7%). Two patients (7%) have positive lymph nodes. PSA was <0.2 ng/mL at 6-12 months for 37 patients (88%). Four patients had a biological recurrence. One patient had a metastatic disease (neuroendocrine component). Nine patients had complementary radiotherapy. Six patients had PSM (3 with a postoperative PSA>0.2 ng/ml), two patients had positive lymph nodes, two had a biological recurrence, one had a metastatic extension (neuroendocrine contingent).

Thirty-seven (88%) patients were continent: 27 (64%) did not need any pads, 10 (24%) needed 1 pad/day. Five (12%) patients were incontinent: 2 (5%) patients needed 2 pads/day and 3 (7%) patients needed 3 or more pads/day (3; 7%)).

Out of the 36 patients with available data, 4 patients (11 %) recovered potency without treatment, 23 (64%) with appropriate treatment (5 with phosphodiesterase type 5 inhibitors, 11 with intra-cavernous injections; data was missing for 7 patients). Nine patients did not recover potency. It should be underlined that 10 patients (28%) had an erectile dysfunction before prostatectomy.

Perception of “a difficult surgery” was not significantly associated with positive margins on the VTP-treated side (4 patients versus 3, p=0.672) or on the non-treated side 1 (3 versus 1, p=1) (table 4). A prior bilateral treatment was not significantly correlated with surgical difficulties (p=0.27), neither two distinct procedures of VTP (p=1), nor surgical approach (p=0.817).
Positivity of surgical margins was not significantly associated with NS (p=0.163), nor with number of VTP procedures (p=0.768).

DISCUSSION:

TOOKAD® padeliporfin obtained in September 2017 the marketing authorisation by the European Committee for Medicinal Products for Human Use in first intention for patients with low risk prostate cancer and a 10-years life expectancy. In this setting, VTP has demonstrated its safety, and efficacy compared to active surveillance [5]. In our study, we included all patients of Lebdai et al. study [12] and our findings confirm that performing a prostatectomy after VTP was safe and feasible in all the cases.

Contrary to other series of salvage prostatectomy following focal therapy, surgery after VTP seems feasible [9,13]. Surgeons reported that lateral fibrosis made the dissection of nerve bundles difficult on the VTP treated-side. They also reported posterior fibrosis with adherences to the rectum, leading to pass in rectum fibres in two cases. However, despite these difficulties, no rectal injuries and no anastomotic strictures occurred [14]. Operative time and blood loss, were similar to primary prostatectomy[15,16].

Hospital stay and time of urethral catheterization was standard [16]. Contrary to the previous series [12], we did not find any significant association between bilateral treatment and surgical difficulties.

A second concern is regarding oncologic outcomes. Our study has shown a relatively high positive lymph node rate in this cohort, for which lymphadenectomy is usually not recommended because of a risk of less than 7%. Some authors have reported similar rates in low-risk cohorts[17,18]. Positive surgical margins of 31%, was similar to the literature [5] but also higher that what might be expected in this selected group of patients with low risk cancer prostate cancer (PSA≤10 ng/ml, T2a and Gleason score ≤7 (3 + 4)). This could be explained by the frequency of bilateral involvement and extracapsular extension. This might be due to the fact that no second biopsy was mandatory at the inclusion. This underlines the need to improve our initial staging by using more precise tools such as MRI guided biopsies[19,20]. As pre-RP MRIs were only available in a few centres, we were unable to include imaging data. Therefore, some patients might have been under staged or graded. One of the cases is particularly obvious: the patient developed metastasis after RP despite the fact that only 4 months passed between VTP and surgery. The final pathology revealed a neuroendocrine differentiation, which had not been diagnosed on biopsy. Of course, inaccurate staging of the initial tumour is a hinderance for appropriate patient selection for both focal therapies and active surveillance. We are confident that contemporary diagnostics aid in better treatment recommendations for individual patients.

In the treated parts, anatomopathological examination of the prostate finds fibrous changes as well as zones of coagulation necrosis.

At present there has been no difference for oncologic control and recovery of continence or erectile function between surgical approaches [21]. However, we may ask ourselves whether the robot-assisted surgery may ease the NS. Only two patients had a bilateral NS with open surgery, although NS was not associated with positive margins. NS seemed technically feasible even on the treated side in 14

patients. Only one of these patients have had a positive surgical margin subsequently . Rate of surgical margins and quality of NS depends on surgeons' experience in particular with robot-assisted surgery. No decision for open, laparoscopic or robotic approach was made upon stage, morbidity or age of the patients.

Table 5 shows that our continence results were similar to those of primary prostatectomy [22] and salvage prostatectomy in literature [23]. According to Ficarra et al [16], the 12 months urinary continence rate ranges from 48% to 93.7% after primary prostatectomy. In our series, one of the patients who had incontinence had a follow-up of only 3 months after prostatectomy, which is not enough to reach his definitive continence status. In the same way, the rate of potency was similar than after primary prostatectomy. Carlsson et al [22] reported potency in 44% of men with appropriate treatment after prostatectomy for very low risk PCa. Recently, a prospective study reported an erectile dysfunction of 70-75% in open and robot assisted primary RP [24]. If we focus on results of salvage prostatectomy our results seems to be better [9,13,25–27].

We acknowledge the following limitations of this study: the small number of patients, retrospective aspect of our data, high number of centers, the fact that no standardized questionnaires were used to assess the functional outcomes and the relatively short follow-up. The surgical difficulty was evaluated by the surgeons who operated on the patients, based on their or notes. Although there is risk of a "recall bias", we felt that this rough assessment was reliable because the procedures were recent and the fact that there were not that many patients with this indication.

However, this is the largest series of salvage RP post-VTP to-date.

Given the uncertainty of the effect of radiotherapy on treated tissues, surgery was chosen in all cases as salvage treatment but other options such as radiotherapy should be explored.

CONCLUSION

Salvage RP after TOOKAD® vascular targeted photodynamic therapy was feasible, safe and efficient to treat locally recurrent PCa in most cases. Short-term oncologic and functional outcomes

were comparable to regular radical prostatectomies, but long-term follow-up is needed for oncologic outcomes.

BIBLIOGRAPHY:

1. Mottet N, Bellmunt J, Bolla M, et al: EAU-ESTRO-SIOG Guidelines on Prostate Cancer. Part 1: Screening, Diagnosis, and Local Treatment with Curative Intent. Eur. Urol. 2017; 71: 618–629.

2. Lee DJ, Mallin K, Graves AJ, et al: Recent Changes in Prostate Cancer Screening Practices and Epidemiology. J. Urol. 2017; 198: 1230–1240.

3. Hamdy FC, Donovan JL, Lane JA, et al: 10-Year Outcomes after Monitoring, Surgery, or Radiotherapy for Localized Prostate Cancer. N. Engl. J. Med. 2016; 375: 1415–1424.

4. Loeb S, Bjurlin MA, Nicholson J, et al: Overdiagnosis and overtreatment of prostate cancer. Eur. Urol. 2014; 65: 1046–1055.

5. Azzouzi A-R, Vincendeau S, Barret E, et al: Padeliporfin vascular-targeted photodynamic therapy versus active surveillance in men with low-risk prostate cancer (CLIN1001 PCM301): an open-label, phase 3, randomised controlled trial. Lancet Oncol. 2017; 18: 181–191.

6. Azzouzi AR, Barret E, Bennet J, et al: TOOKAD® Soluble focal therapy: pooled analysis of three phase II studies assessing the minimally invasive ablation of localized prostate cancer. World J. Urol. 2015; 33: 945–953.

7. Rouvière O, Chapelon J-Y, Crouzet S, et al: Prostate Cancer Focal Therapy: Just Because You Can Does Not Mean You Should. Eur. Urol. 2017; 71: 35–36.

8. Valerio M, Emberton M and Ahmed HU: Focal Therapy Will Become a Standard Option for Selected Men With Localized Prostate Cancer. J. Clin. Oncol. 2014; 32: 3680–3681.

9. Leonardo C, Franco G, De Nunzio C, et al: Salvage laparoscopic radical prostatectomy following high-intensity focused ultrasound for treatment of prostate cancer. Urology 2012; 80: 130–133.

10. Gotto GT, Yunis LH, Vora K, et al: Impact of prior prostate radiation on complications after radical prostatectomy. J. Urol. 2010; 184: 136–142.

11. Epstein JI, Zelefsky MJ, Sjoberg DD, et al: A Contemporary Prostate Cancer Grading System: A Validated Alternative to the Gleason Score. Eur. Urol. 2016; 69: 428–435.

12. Lebdai S, Villers A, Barret E, et al: Feasibility, safety, and efficacy of salvage radical prostatectomy after Tookad® Soluble focal treatment for localized prostate cancer. World J. Urol. 2015; 33: 965–971.

13. Lawrentschuk N, Finelli A, Van der Kwast TH, et al: Salvage radical prostatectomy following primary high intensity focused ultrasound for treatment of prostate cancer. J. Urol. 2011; 185: 862–868.

14. Chade DC, Eastham J, Graefen M, et al: Cancer control and functional outcomes of salvage radical prostatectomy for radiation-recurrent prostate cancer: a systematic review of the literature. Eur. Urol. 2012; 61: 961–971.

15. Ficarra V, Novara G, Ahlering TE, et al: Systematic review and meta-analysis of studies reporting potency rates after robot-assisted radical prostatectomy. Eur. Urol. 2012; 62: 418–430.

16. Ficarra V, Novara G, Artibani W, et al: Retropubic, laparoscopic, and robot-assisted radical prostatectomy: a systematic review and cumulative analysis of comparative studies. Eur. Urol. 2009; 55: 1037–1063.

17. Salomon L, Peyromaure M, Fromont G, et al: [Lymphadenectomy and prostate cancer: a statement of the committee of cancerology of the French Association of Urology]. Progres En Urol. J. Assoc. Francaise Urol. Soc. Francaise Urol. 2012; 22: 510–519.

18. Weckermann D, Wawroschek F and Harzmann R: Is there a need for pelvic lymph node dissection in low risk prostate cancer patients prior to definitive local therapy? Eur. Urol. 2005; 47: 45–50; discussion 50-51.

19. Cheng L, Slezak J, Bergstralh EJ, et al: Preoperative prediction of surgical margin status in patients with prostate cancer treated by radical prostatectomy. J. Clin. Oncol. Off. J. Am. Soc. Clin. Oncol. 2000; 18: 2862–2868.

20. Park BH, Jeon HG, Jeong BC, et al: Influence of magnetic resonance imaging in the decision to preserve or resect neurovascular bundles at robotic assisted laparoscopic radical prostatectomy. J. Urol. 2014; 192: 82–88.

21. Rozet F, Hennequin C, Beauval J-B, et al: [CCAFU french national guidelines 2016-2018 on prostate cancer]. Progres En Urol. J. Assoc. Francaise Urol. Soc. Francaise Urol. 2016; 27 Suppl 1: S95–S143.

22. Carlsson S, Jäderling F, Wallerstedt A, et al: Oncological and functional outcomes 1 year after radical prostatectomy for very-low-risk prostate cancer: results from the prospective LAPPRO trial. BJU Int. 2016; 118: 205–212.

23. Linares Espinós E, Sánchez-Salas R, Sivaraman A, et al: Minimally Invasive Salvage Prostatectomy After Primary Radiation or Ablation Treatment. Urology 2016; 94: 111–116.

24. Haglind E, Carlsson S, Stranne J, et al: Urinary Incontinence and Erectile Dysfunction After Robotic Versus Open Radical Prostatectomy: A Prospective, Controlled, Nonrandomised Trial. Eur. Urol. 2015; 68: 216–225.

25. Saeedi Y, Pop M and Jacqmin D: [Salvage radical prostatectomy for brachytherapy failure: preliminary results]. Progres En Urol. J. Assoc. Francaise Urol. Soc. Francaise Urol. 2014; 24: 266–270.

26. Chade DC, Eastham J, Graefen M, et al: Cancer control and functional outcomes of salvage radical prostatectomy for radiation-recurrent prostate cancer: a systematic review of the literature. Eur. Urol. 2012; 61: 961–971.

27. Zargar H, Lamb AD, Rocco B, et al: Salvage robotic prostatectomy for radio recurrent prostate cancer: technical challenges and outcome analysis. Minerva Urol. E Nefrol. Ital. J. Urol. Nephrol. 2017; 69: 26–37.

28. Wallerstedt A, Carlsson S, Steineck G, et al: Patient and tumour-related factors for prediction of urinary incontinence after radical prostatectomy. Scand. J. Urol. 2013; 47: 272–281.

29. Donovan JL, Hamdy FC, Lane JA, et al: Patient-Reported Outcomes after Monitoring, Surgery, or Radiotherapy for Prostate Cancer. N. Engl. J. Med. 2016; 375: 1425–1437.

30. Orré M, Piéchaud T, Sargos P, et al: Oncological and functional results of robotic salvage radical prostatectomy after permanent brachytherapy implants. Cancer Radiother. J. Soc. Francaise Radiother. Oncol. 2017; 21: 119–123.

Table 1: Initial characteristics of patients

	Total **(n= 42)**
Data pre-VTP	
Age at the time of VTP (years)	63 (60-65)
Clinical T-stage***** :	
T1a	1 (2.5)
T1c	36 (90)
T2a	3 (7.5)
Prostatic volume (mL)	35 (30-46)
Group(ISUP)	1
Number of positive biopsies	2 (1-2)
Number of treated lobes :	
1 lobe	31 (74)
2 lobes	11 (26)
Second procedure of VTP	5 (12)
Data pre-PR	
Age at the time of RP (years)	65 (61-67)
PSA nadir (ng/mL)	2.9 (1.9-5.1)
PSA before prostatectomy (ng/mL)	5.9 (3.2-7.9)
Positive biopsies after VTP :	
Cancer in the treated lobe	25 (63)
Cancer in the non-treated lobe	27 (67)
Bilateral cancer	14 (33)
Number of positive biopsies	3 (2-4)
Group 1	15 (42)
Group 2	11 (31)
Group 3	8 (22)
Group 4	2 (6)

Data are median (interquartile range IQR) or number (percentage %) unless otherwise indicated.
***data was missing for two patients.**
VTP: vascular targeted photodynamic therapy
ISUP : International Society of Urological Pathology
TNM: tumour, node, metastasis
PSA: Prostate specific Antigen

Table 2: Per and immediate post-operative data for radical prostatectomy

	All RP (n=42)	Robot assisted surgery (n=16)	Laparoscopic surgery (n=6)	Open surgery (n=20)
Per-operative data				
Operative time (min)	180 (150-223)	223 (179-243)	169 (129-225)	158 (150-180)
Blood loss (mL)	200 (155-363)	200 (98-238)	200 (125-200)	325 (213-500)
Transfusion (number of patients)	1 (3)	0 (0)	0 (0)	1 (5)
Conversion	0 (0)	0 (0)	0 (0)	0
Per-operative complication	1 (2)	0 (0)	0 (0)	1 (5)
Nerve sparing :				
Unilateral	4 (10)	2 (12.5)	2 (33.3)	0 (0)
Bilateral	10 (24)	6 (37.5)	2 (33.3)	2 (10)
No nerve sparing	28 (67)	8 (50)	2 (33.3)	18 (90)
Lymphadenectomy	30 (71)	8 (50)	3 (50)	19 (95)
Difficult surgery	13 (31)	6 (37.5)	2 (33)	14 (70)
Post-operative data				
Urethral catheterization (days)	7 (7-8)	7 (7-9)	7 (7-9)	7 (7-7)
Immediate complication	5 (12)	0 (0)	0 (0)	5 (25)
Hospital stay (days)	7 (5-8)	5 (3-7)	5 (4-6)	7 (7-8)

Data are median (interquartile range IQR) or number (percentage %) unless otherwise indicated.

Table 3: Oncological outcomes after radical prostatectomy

Characteristics	Number of patient n/N (%)
Stage post RP :	
T2a	4/42 (9.5)
T2b	4/42 (9.5)
T2c	21/42 (50)
T3	13/42 (31)
Positive lymph node	2/29 (7)
Surgical margin status :	
PSM	13/42 (31)
PSM on the treated side	7/35 (20)
PSM status pT2c	5/21 (24)
PSM status pT3	7/12 (58)
PSM status on the treated side if NS	1/14 (21)
Gleason Score (ISUP group) :	
Group 1	8/42 (19)
Group 2	24/42 (57)
Group 3	7/42 (17)
Group 4	1/42 (2)
Group 5	2/42 (5)
Post-operative PSA :	
PSA <0.1 ng/mL*	37/42 (88) **
Last PSA <0.2 ng/mL *	38/42 (90)

*median PSA (IQR) at
**Four PSA were < 0.1 ng/mL at 6 months.
PSM: positive surgical margins
RP: radical prostatectomy
NS: Nerve Sparing
ISUP : International Society of Urological Pathology
PSA: prostatic specific antigen

Table 4: Correlation between surgical difficulties, localisation, margins, number of prior VTP and surgical approach.

	Surgical difficulties		P value
	Easy n=29	Difficult n=13	
Pre-operative localisation			
Bilateral	4 (13.8)	4 (30.8)	0.226
Unilateral	25 (86.2)	9 (69.2)	
Margins			
Positive on the treated side	4 (16)	3 (23.1)	0.672
Positive on the non-treated side	3 (12)	1 (7.7)	1
Prior VTP			
Initial unilateral treatment	23 (79.3)	8 (61.5)	0.27
Initial bilateral treatment	6 (20.7)	5 (38.5)	
One VTP	25 (86.2)	12 (92.3)	1
Two VTP	4 (13.8)	1 (7.7)	
Surgical approach			
Robotic	9 (34.6)	4 (46.2)	0.817
Laparoscopic	4 (15.4)	2 (15.4)	
Open surgery	13 (50.0)	5 (38.5)	

	Surgical margins		P value
	Negative n=29	**Positive n=13**	
Surgical approach			
Open surgery	**10 (34.5)**	**8 (61.5)**	**0.141**
Laparoscopic surgery	**5 (17.2)**	**3 (23.1)**	
Robotic surgery	**14 (48.3)**	**2 (15.4)**	
Nerve sparing			
No nerve sparing	**18 (62.1)**	**10 (76.9)**	**0.163**
Unilateral nerve sparing	**3 (10.3)**	**1 (7.7)**	
Bilateral nerve sparing	**8 (27.6)**	**2 (15.4)**	
Number of VTP procedures*			
One procedure	**21 (72.4)**	**6 (46.2)**	**0.768**
Two procedures	**8 (27.6)**	**7 (53.8)**	

*Contralateral treatment or salvage VTP
VTPPT: vascular targeted photodynamic therapy
Test de Fisher. Values are presented as number (%).

Table 5: Functional outcomes in our study compared with data from literature

Study	Procedure type (number of patient)	Criterion	Results at 12 months (%)
Our study	RRP/RALP/LRP (n=41)	≤ 1pad	88%
		No pad	64 %
Primary prostatectomy			
Carlsson et al. [22]	RALP vs RRP (n=315)	<1 pad changed per/d	84%
		No pad	72%
Wallerstedt et al. [28],	RALP vs RRP (n=1360)	No Pad	66%
Haglind et al. [24],	RALP VS RRP (n=2431)	<1 pad	79 %
Donovan et al.[29]	RRP/RALP/LRP (n=553)	<1 pad/day	70%
Salvage Prostatectomy			
Leonardo et al.[9]	LRP (n=13) after HIFU	No pad	69%
Lawrentschuk et al. [13]	RRP (n=15) after HIFU	No pad	60%
Orré et al. [30]	RARP (n=7) after brachytherapy	No pad	57%
Linares Espinos et al. [23]	LRP/RARP (n=12/16) after ERBT (n=6), brachytherapy (n=3) VTP (n=1), HIFU (n=6), cryotherapy (n=12)	No pad	57%
		≤1 pad	67%

RALP : robot assisted laparoscopic prostatectomy
RRP : radical retropubic prostatectomy
LRP : laparoscopic radical prostatectomy
EBRT : external beam radiation therapy
HIFU : High Intensity Focused Ultrasound

Abreviations :

VPT: vascular photodynamic therapy

RP : radical prostatectomy

PCa : prostate Cancer

NS : nerve sparing

PSM : positive surgical margins

RALP : robot assisted laparoscopic prostatectomy

RRP : retropubic radical prostatectomy

HIFU : high intensity focal therapy