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Oncologic and functional outcomes one year after radical prostatectomy for very low risk prostate cancer. Results from the prospective LAPPRO trial

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Abstract

Objectives—To analyse oncological and functional outcomes 12 months after treatment of very low risk prostate cancer with radical prostatectomy in men who could have been candidates for active surveillance.

Patients and Methods—A prospective study of all men with very low risk prostate cancer who underwent radical prostatectomy at 14 participating centres. Validated patient questionnaires were collected at base line and after 12 months by independent health-care researchers. Biochemical recurrence (BCR) was defined as PSA ≥ 0.25 ng/ml or treatment with salvage radiotherapy or treated with hormones. Urinary continence was defined as "less than one pad changed per 24 hour". Erectile function was defined as ”erection hard enough for penetration more than half of the time after sexual stimulation”. Changes in tumor grade and stage were obtained from pathology reports. We show descriptive frequencies and proportions having each outcome in various subgroups. Fisher’s exact test was used to assess differences between the age groups.

Results—Of the 4003 men in the LAPPRO cohort, 338 men fulfilled the preoperative national criteria for very low risk prostate cancer. Adverse pathology outcomes included: upgrading,

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Conflicts of Interest

All other authors have nothing to disclose.

defined as pT3 or postoperative Gleason sum ≥ 7, was present in 35% (115/333), positive surgical margins, 16% (54/329). Only 7/329 men (2.1%) had PSA concentration > 0.1 ng/ml 6–12 weeks postoperatively. Erectile function and urinary continence were 44% (98/222) and 84% (264/315) 12 months postoperatively. Trifecta defined as preoperative potent and continent men that remained potent and continent with no BCR was at 12 months 38 % (84/221).

Conclusions—Our prospective study of men with very low risk prostate cancer undergoing open or robotic radical prostatectomy showed favourable oncological outcome in about two-thirds. About 40 per cent did not suffer from surgically induced urinary incontinence or erectile dysfunction 12 months postoperatively. These results provide additional support for the use of active surveillance in men with very low risk prostate cancer, however the group of men with risk of upgrading and upstaging is not negligible. Improved stratification is still an urgently needed.

Keywords

prostate cancer; radical prostatectomy; erectile dysfunction; urinary incontinence; very low risk prostate cancer

INTRODUCTION

The first principle of medical ethics as stated by Hippocrates, the father of Western medicine, is *primum, non nocere* – “first of all, do not harm”. This is highly relevant in the discussion of surgical treatment of very low risk prostate cancer. Early detection of prostate cancer is associated with the diagnosis of a considerable proportion of cancers that are indolent, and if left untreated are unlikely to cause symptoms or affect survival[1]. However, many of these low risk prostate cancer patients do not receive active surveillance as a first line of treatment. Hoffman and co workers recently reported that a patient diagnosed with low risk cancer in USA is more likely to receive the treatment that his urologist most commonly performs[2]. How the physician communicates a prostate cancer diagnosis and discusses the severity of the disease and management options with a patient will influence whether active surveillance will be the first treatment of choice or not[3]. In this context of decision making, appropriate communication with the patient is an essential component of the active-surveillance strategy to reduce the psychological burden of living with untreated cancer. It is important that a man in Sweden diagnosed with very low risk prostate cancer and choosing treatment with radical prostatectomy is informed about the expected outcomes. We therefore extracted men diagnosed with very low risk prostate cancer who could have been candidates for active surveillance and were included in the prospective LAPPRO trial[4], which includes data on men treated with radical prostatectomy from 14 Swedish centers, and sought to determine the oncological and functional results 12 months after radical prostatectomy.

PATIENTS AND METHODS

Trial design

The LAPPRO trial with its prospective study design, included patients from 14 participating centres in Sweden. The hospitals and the surgeons are a mixture of high and low volume hospitals and surgeons, which mimics the reality facing those Swedish patients with low risk

prostate cancer who wish to have surgery for prostate cancer. Swedish health care is organized by county, so these patients were not free to seek health care across county borders for one or more perhaps personal reasons. Thus for the majority of participants, geographical location was the deciding factor behind the choice of hospital and surgeon. The design and data collection of the LAPPRO trial have been described previously[4,5,6].

Participants

The LAPPRO trial collected data from a total of 4003 men from 14 participating centres between September 1, 2008 and November 7, 2011. In this study patients had to meet the following inclusion criteria for **very low risk prostate cancer** described in the Swedish national guidelines: T1c, prostate-specific antigen (PSA) concentration less than 10 ng/ml, PSA density < 0.15 ng/ml^2, Gleason sum 6 in up to 4 positive biopsy cores with a total biopsy cancer length of ≤ 8 mm, in excess of the inclusion criteria for the LAPPRO trial age less than 75 years, ability to read and write in Swedish, written informed consent and no signs of distant metastasis.

Data collection

Clinical record forms (CRFs) were filled out before, during and at 6–12 weeks, 12 and 24 months after surgery. Patient-reported data were collected before and 3, 12 and 24 months after surgery via validated questionnaires administered and collected by a neutral third party[5]. The study questionnaires reporting patient outcomes have the same clinometric approach as a previous randomized controlled trial and more than twenty large-sized data collections of cancer survivors[789]. The validation of the questionnaires and the pilot study performed before study-start has been described earlier[5]. Study staff visited the centres to monitor data reported in CRFs in comparison with original data in hospital records.

Outcomes

The outcomes considered include adverse pathology as reported in the CRFs and functional outcomes 12 months after surgery as reported by the patients through questionnaires. Adverse pathology outcomes included upgrading, defined as pT3 or postoperative Gleason sum of ≥ 7, positive surgical margins and PSA > 0.1 ng/ml 6–12 weeks postoperatively. Positive surgical margin was based on CRFs: *“no information”, “negative”, “focal”, “extensive” or “other”*. In the analysis, we combined focal and extensive into “positive surgical margin” status. We also analysed biochemical relapse (BCR) defined as PSA ≥ 0.25 ng/ml or treatment with salvage radiotherapy or treated with hormones up to 12 months later. The reason for choosing a cut off level of PSA ≥ 0.25 ng/ml instead of > 0.20 ng/ml was that some centres reported PSA with only one decimal.

Functional outcome was measured as self-reported urinary continence and erectile function. The questionnaire included questions about urinary function and erectile function, most of which had been used earlier[1011]. For urinary continence we asked, “How many times do you change pad, diaper or other sanitary protection during a typical 24 hours?” The available responses were *“Not applicable, I do not use pad, diaper or a sanitary protection”, “Less than once per 24 hours, i.e. an occasional pad”, “About once per 24 hours”, “About two to three times per 24 hours”, “About four to five times per 24 hours” or “About six times or*

more per 24 hours". Urinary continence was defined as *"Less than one pad changed per 24 hour, i.e. an occasional pad"* at 12 months. For self-reported erectile function, we used a Swedish translation of question three from the International Index of Erectile Function score[12]: "When you had erections with sexual stimulation, how often was your erection hard enough for penetration during the last 3 months?", answer categories: "*No sexual activity", "Never hard enough for penetration", "Less than half of the times", "More than half of the times/always"*. Erectile function was defined as *"Erection hard enough for penetration more than half of the times after sexual stimulation"* at 12 months. The questionnaires included further questions about urinary continence/incontinence (Table 3b) and erectile function/dysfunction (Table 3a, 3b and 4). We defined trifecta cases at 12 months as those men with no BCR or salvage radiotherapy and being urinary continent and having erectile function.

Statistical analysis

Tables 1–3 show descriptive frequencies and proportions having each outcome in various subgroups. To compare outcomes between younger and older men, Table 4 shows the corresponding outcomes split between men below and above 60 years of age at surgery. Fisher's exact test was used to assess differences between the age groups. All tests were done two-sided at the 5% significance level. Data management and calculations were performed using SAS software (version 9.4, SAS Institute Inc., Cary NC, USA).

RESULTS

The median age of men in the study population was 60.7 year (range 39–74 years). Table 1 shows demographics and patient characteristics. Of the 4003 men from 14 participating centres in the LAPPRO overall cohort, 338 men fulfilled the criteria for very low risk prostate cancer. Return of the CRFs varied from 97% to 99% per cent and the response rate for questionnaires from 89% to 99%.

Adverse pathology, PSA and BCR

Upgrading to stage pT3 or postoperative Gleason sum of ≥ 7 was present in 34% (115/333), positive surgical margins in 16% (54/329) and PSA > 0.1 ng/ml 6–12 weeks postoperative in 2.1% (7/329) of the patients and 2.4% (8/334) had BCR at 12 months (5 patients had salvage radiotherapy and none was treated with hormones). (Table 2).

Urinary continence at 12 months after operation

Urinary continence was reported by 84% (264/315) 12 months postoperatively (Table 3a). When the answers to additional questions concerning details of urinary leakage were taken into account and the various subgroups were analysed, the proportion of patients classified as being urinary continent ranged from 47.3 % (pad free, leakage free) to 92.6% (postoperative change of pad less than once per 24 hours in the subgroup of patients 39–59 years old who preoperatively reported change of pad less than once per 24 hours and had been operated with bilateral nerve-sparing operation) (Table 3a and Table 4).

Recovery of erectile function

Erectile function was reported by 44% of the patients (98/222) one year after surgery (Table 3b), Classification of erectile function by different definitions and different age groups ranged from 16% (IIEF>21) to 50 % (postoperative capable of penetration more than half of the times in the subgroup of patients 60–74 years old who were preoperatively capable of penetration more than half of the times operated with bilaterally nerve-sparing operation) (Table 3b and Table 4). In our study men who answered the questionnaires about their erection 170/312 (54.7%) had used PDE5 inhibitors and 39/312 (12.8%) had used intracavernosal injections.

Trifecta

Among patients with preoperative satisfying erectile and urinary functions, 40% (75/189) had preserved functions 12 months after surgery and 39% (73/189) was trifecta at 12 months (Table 3c).

DISCUSSION

This study to evaluate outcomes after surgery in Sweden in men with very low risk prostate cancer showed about two-thirds with favourable oncological outcome and only 40 per cent without surgery-induced urinary incontinence or erectile dysfunction 12 months postoperatively.

Vellekoop and co-workers performed a registry-based study in the NPCR (National Prostate Cancer Register of Sweden) and showed a similar proportion of adverse pathology after radical prostatectomy in more than 2000 candidates for active surveillance (33% with John Hopkins active surveillance protocol)[13]. Hajj and co-workers found a slightly higher proportion of unfavourable oncological outcome in 625 patients who fulfilled PRIAS (Prostate Cancer Research International Active Surveillance) criteria and had undergone immediate radical prostatectomy (50%)[14]. Hong and co-workers, who used a confirmatory biopsy to reassess eligibility for active surveillance, found a somewhat lower proportion of unfavourable oncological outcome (28%) after a median 1.7 years of active surveillance before undergoing radical prostatectomy[15]. By using a repeat biopsy within 3 months of the first biopsy before starting on active surveillance, Berglund and co-workers found upgrading to Gleason 7 or more in 17% of the 104 patients primarily eligible for active surveillance and Shapiro and Johnstone found as high as 42% Gleason upgrading using repeat biopsies as reported in a literature review in 2012[1617]. To decrease misclassification due to sample bias, recent advances in multi-parametric magnetic resonance imaging (mpMRI) suggest a high negative predictive value for the presence of clinically significant disease in patients eligible for active surveillance[18], including the use of targeted biopsies to rule out significant disease in cases with positive findings from mpMRI. However, the proportion of adverse pathology after radical prostatectomy in very low risk prostate cancer is probably an imperfect predictor of long term survival, since the PIVOT trial showed no survival benefit with radical prostatectomy compared to observation for the entire low risk group after 12 years of follow up[19]. Furthermore, in the 224 (23%) of the patients in the Göteborg screening trial classified

as very low risk and managed with active surveillance, no metastatic disease and no deaths from prostate cancer have occurred during a median follow up of 6 years[20].

To our knowledge, very little is known about functional outcome after radical prostatectomy in very low risk prostate cancer patients. Theoretically, these patients are ideal candidates for surgery with optimal feasibility for preservation of urinary and erectile functions. Considering the low possibility of survival benefits of surgery for these men with very low risk prostate cancer, as mentioned above, one might argue that "pad-free and leakage-free urinary continence" would be the appropriate definition of continence from the patient's perspective, as indicated when taking the patient's bother into account[19,21]. When using this definition, only about half of the patients who met these criteria preoperatively retained continence 12 months postoperatively. The levels of 12 month postoperative continence vary between 69–96% in the existing literature, levels similar to our results[22]. However, the average continence rate according to a review of Ficarra et al. using the definition pad free leakage was 84%, compared to 72% in the present study[22]. A spectrum of various surgeon's experience and of high and low volume hospitals in this multi-centre study could presumably explain some of the difference[23]. On the other hand, in a previous report from the LAPPRO trial, Wallerstedt and co-workers analysed predictors for urinary incontinence in the first 1529 men included in the cohort (all risk groups) and found a continence rate of only 76% using the definition *"Less than one pad changed per 24 hours"* at 12 months, which was less compared to the rate in this cohort of very low risk cancers, 84%[24]. One explanation for this higher incontinence rate is probably that when surgery is performed on a cohort of patients consisting of all three subgroups –low-risk, intermediate-risk, and high-risk prostate cancer, the feasibility of bilateral neurovascular bundle preservation will decrease (72% to 46–53%) and thereby contribute to higher rates of urinary incontinence[25].

A recovery of erectile function in less than 50% of preoperatively potent men at 12 months is lower than reported in a recent review of the literature reporting mean values of erectile function recovery of 70% at 12 months after surgery[26]. A recovery of erectile function in 37% (all men) is, however, higher than reported recently in a study using the same definition of self-reported erectile function used in the LAPPRO trial (25–30% at 12 months)[4]. Van den Bergh and co-workers compared sexual function in a cohort of patients who fulfilled PRIAS criteria (Prostate Cancer Research International Active Surveillance) and had been treated with active surveillance with a cohort of patients from European Randomized Study of Screening for Prostrate Cancer (ERSPC) treated with RP. The study of the RP treated group that was, however, not strictly a very low risk prostate cancer group (T2 prostate cancers included), found that only 14% of the men were sexually active without erectile problems at 18 months compared to 70% of the men in the non-operated group[27]. Erectile function recovery appears to be higher in single centre, single surgeon series compared with multi-centre, multi-surgeon series[28]. Variation in the nature of the population studied, data acquisition, and definition of baseline and postoperative erectile function are factors that may influence the results[28]. Unfortunately, also selection bias might be a problem in some studies that are made on a highly selected fraction of patients. Potency results from such subgroups cannot be accurately extrapolated to the general population of men having surgery as treatment for prostate cancer. We believe, however that there is a rather high probability of generalizability for the results from our study of all men with a very low risk

prostate cancer having a radical prostatectomy as primary treatment in the LAPPRO trial (with the participating 14 hospitals in Sweden).

The strengths of our study include the sample size, high participation and response rates, the neutral third-party approach and the data collection method with prospectively collected validated questionnaires and the multicentre study design that possibly better reflects average surgical competence in Sweden. At the same time that the multicentre study design is regarded as a strength, it might also be seen as a limitation since no distinction was made in the analysis between results in high- and low-volume centres and between high- and low-volume surgeons. An analysis of oncological and functional results from a single Swedish high-volume surgeon might have been of interest. However, the average patient with very low risk prostate cancer will most likely not meet a surgeon with high volume experience. Another limitation is the absence of PSA history for this cohort of very low risk prostate cancer that underwent surgery. It is common to advise against active surveillance in men with a PSA doubling time (PSADT) < 3 years[29,30] or if there is a rise in PSA of more than 2 ng/ml/y before starting active surveillance[31,32]. It cannot be entirely ruled out that the lack of data on PSA history, as well as the absence of a repeat biopsy, may influence the extent of adverse pathology after surgery in this study.

In a future setting, mpMRI in conjunction with targeted biopsies could play an important role in reducing the proportion of very low risk prostate cancers found. Patients, who despite use of these new methods, turn out to have a very low risk prostate cancer should instead of having surgery, to avoid overtreatment and to preserve sexual and urinary functions, be monitored in a active surveillance program including mpMRT to better rule out misclassification or progressive disease[33]. For these few men who, in spite of high quality patient-doctor communication about very low risk prostate cancer risks and expected outcomes with treatment, choose to have surgery, assignment whenever possible to a surgeon who is particularly skilled in correctly preserving both neurovascular bundles is recommended.

CONCLUSION

From a surgeon’s perspective, a man with very low risk prostate cancer is the ideal candidate for surgery with optimal potential for perfect oncological outcome and feasibility for preservation of urinary and erectile functions. From this study however, we can conclude that choosing surgery as the primary treatment for this set of men in Sweden, will result in a favourable outcome as concerns the cancer for about two thirds of the cases, but is likely to jeopardize a man’s sexual and urinary health to a great extent. These results therefore provide additional support for the use of active surveillance in men with very low risk prostate cancer, however the group of men with risk of upgrading and upstaging is not negligible. Improved stratification in the future with more advanced mpMRI and target biopsies is urgently needed.

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Table 1

Baseline patient characteristics

Characteristic	Very low risk prostate cancer (N=338)
Pre-operative characteristics	
Age at surgery (years)	
Median (range)	60.7 (39 – 74)
PSA (ng/ml) **preoperatively**	
Median (range)	4.6 (0.5–9.9)
IPSS score preoperatively	
Mild 0–7	147 (51.0)
Moderate 8–19	116 (40.3)
Severe 20–35	25 (8.7)
Level of education	
University/college	123 (42.4)
Technical training school	36 (12.4)
High school	91 (31.3)
Elementary school	36 (12.4)
Other	4 (1.4)
Marital status	
Partner	278 (95.9)
Single	12 (4.1)
BMI preoperatively (kg/m^2)	
< 25	98 (34.1)
25–30	166 (57.8)
> 30	23 (8.0)
Previous TUR-P	
Yes	7 (2.5)
No	270 (97.5)
Previous coronary bypass	
Yes	5 (1.8)
No	280 (98.2)
Previous abdominal surgery	
Yes	53 (18.6)
No	232 (81.4)
Previous AMI	
Yes	1 (0.3)
No	290 (99.7)
Hypertonia	
Yes	72 (24.7)

Characteristic	Very low risk prostate cancer (N=338)
No	219 (75.3)
Angina Pectoris	
Yes	1 (0.3)
No	290 (99.7)
Heart Failure	
Yes	1 (0.3)
No	290 (99.7)
Diabetes	
Yes	13 (4.5)
No	278 (95.5)
Lung disease	
Yes	6 (2.1)
No	285 (97.9)
Neurologic disease	
Yes	5 (1.7)
No	286 (98.3)
Kidney disease	
Yes	3 (1.0)
No	288 (99.0)
Depression	
Yes	6 (2.1)
No	285 (97.9)

Table 2

Oncological outcome

Adverse Pathology		
#	pT3 and /or postop Gleason score ≥ 7	115/333 (34.5)
	pT3	27/333 (8.0)
	Gleason ≥ 7	105/333 (31.5)
	Gleason score 3+4 = 7	89/105 (84.8)
	Gleason score 4+3 = 7	16/105 (15.2)
	Gleason score ≥8	0/105 (0.0)
Surgical margin status		
	Negative	275/329 (83.6)
	Positive	54/329 (16.4)
Surgical margin status pT2		
Negative		260/302 (86.1)
Positive		42/302 (13.9)
Surgical margin status pT3		
Negative		15/27 (55.6)
Positive		12/27 (44.4)
PSA > 0.1 (ng/ml) 6–12 weeks postoperative		
	Yes	7/329 (2.1)
	No	322/329 (97.9)
BCR (PSA ≥ 0.25 ng/ml or salvage treatment) at 12 months		
	Yes	8/334 (2.4)
	No	326/334 (97.6)

#The primary oncological endpoint in the study.

Table 3

a. Functional outcome, urinary continence		
Various definitions of urinary continence reported by patients before surgery		**no. (%)**
	Pad-free and leakage free	247/290 (85.2)
	Pad-free	287/290 (99.0)
	Change of pad less than once per 24 hours	289/290 (99.7)
Urinary continence (Pad-free and leakage free) reported by patients 12 months after surgery		**no. (%)**
	Pad-free and leakage free	149/315 (47.3)
	Pad-free and leakage free among pre-operatively pad-free and leakage-free patients	123/238 (51.7)
	Pad-free and leakage free among preoperatively pad-free and leakage-free patients with bilateral nerve-sparing	95/178 (53.4)
Urinary continence (Pad-free) reported by patients 12 months after surgery		**no. (%)**
	Pad-free	226/315 (71.7)
	Pad-free among preoperatively pad-free patients	199/276 (72.1)
	Pad-free among preoperatively pad-free patients with bilateral nerve-sparing	154/205 (75.1)
Urinary continence (Change of pad less than once per 24 hours) reported by patients 12 months after surgery		**no. (%)**
	Change of pad less than once per 24 hours	264/315 (83.8)
#	Change of pad less than once per 24 hours among patients with preoperatively change of pad less than once per 24 hours.	234/278 (84.2)
	Change of pad less than once per 24 hours among patients with preoperatively change of pad less than once per 24 hours and bilateral nerve-sparing	181/206 (87.9)

b. Functional outcome, erectile function		
Neurovascular bundle preservation		**no./total no. (%)**
Bilateral, both sides interfascial or intrafascial dissection		242/337 (71.8)
Unilateral		54/337 (16.0)
None		41/337 (12.2)
Preoperative erectile function, reported by patients, different definitions		no./total no. (%)
	IIEF > 21	159/285 (55.8)
	IIEF question 3 ≥ about half the time	233/287 (81.2)
Erectile function reported by patients 12 months after surgery		**no./total no. (%)**
	IIEF > 21	48/308 (15.6)
	IIEF > 21 among patients with bilateral nerve-sparing	40/225 (17.8)
	IIEF > 21 among patients that preoperatively had IIEF > 21	41/150 (27.3)
	IIEF > 21 among patients that preoperatively had IIEF > 21 and with bilateral nerve-sparing	33/121 (27.3)
	IIEF question 3 ≥ about half the time	115/312 (36.9)
	IIEF question 3 ≥ about half the time among patients with bilateral nerve-sparing	96/227 (42.3)
#	IIEF question 3 ≥ about half the time among patients that preoperatively had IIEF question 3 ≥ about half the time	98/222 (44.1)
	IIEF question 3 ≥ about half the time among patients that preoperatively had IIEF question 3 ≥ about half the time and with bilateral nerve-sparing	82/172 (47.7)

c. Functional outcome, Trifecta	
Potent and Continent at 12 months	**no./total no. (%)**

c. Functional outcome, Trifecta		
Potent (IIEF question 3 ≥ about half the time) + continent (Change of pad less than once per 24 hours) among patient that preoperative was potent (≥ about half the time) + continent (Change of pad less than once per 24 hours)		
	Yes	86/221 (38.9)
	No	135/221 (61.1)
Trifecta at 12 months BCR-free or no RT + potent (≥ about half the time) + continent (Change of pad less than once per 24 hours) among all patients		**no./total no. (%)**
	Yes	101/312 (32.4)
	No	211/312 (67.6)
Trifecta at 12 months BCR-free or no RT + potent (≥ about half the time) + continent (Change of pad less than once per 24 hours) among preoperative potent and continent patients.		**no./total no. (%)**
	Yes	84/221 (38.0)
	No	137/221 (62.0)

[#]The primary endpoint for urinary continence in the study.

[#]The primary endpoint for erectile function in the study.

Table 4

Oncological and functional outcome divided in age groups

Characteristic		Age 39–59 year	Age 60–74 year	P value
Adverse Pathology		***no. (%)***	***no. (%)***	
	pT3 and/or Gleason score > 7	*40/121 (33.0)*	*75/212 (35.4)*	0.720
	pT3	*10/121 (8.3)*	*17/212 (8.0)*	1.000
	Gleason ≥ 7	*36 (29.8)*	*69 (32.6)*	
	Gleason score 3+4 = 7	*30/36 (24.8)*	*59/69 (27.8)*	0.841
	Gleason score 4+3 = 7	*6/36 (5.0)*	*10/69 (4.7)*	
	Gleason score ≥ 8	*0/36 (0.0)*	*0/69 (0.0)*	
Surgical margin status				
	Negative	*101/119 (84.9)*	*174/210 (82.9)*	0.757
	Positive	*18/119 (15.1)*	*36/210 (17.1)*	
Surgical margin status pT2				
	Negative	*95/109 (87.2)*	*165/193 (85.5)*	0.732
	Positive	*14/109 (12.8)*	*28/193 (14.5)*	
Surgical margin status pT3				
	Negative	*6/10 (60.0)*	*9/17 (53.0)*	1.000
	Positive	*4/10 (40.0)*	*8/17 (47.0)*	
PSA > 0.1 (ng/l) 6–12 weeks postoperative				
	Yes	*3/120 (2.5)*	*4/209 (1.9)*	0.709
	No	*117/120 (97.5)*	*205/209(98.1)*	
BCR (PSA ≥ 0.25 ng/l) or radiotherapy at 12 months				
	Yes	4/123 (3.2)	4/211 (1.9)	0.507
	No	119/123 (97.8)	207/211 (98.1)	
Neurovascular bundle preservation				
Bilateral, both sides interfascial or intrafascial dissection		*102/124 (82.3)*	*140/213 (65.7)*	**<0.001**
Unilateral		*18/124 (14.5)*	*36/213 (16.9)*	
None		*4/124 (3.2)*	*37/213 (16.9)*	
Erectile function ***(IIEF > 21) reported by patients 12 months after surgery***				
IIEF > 21[a]		*16/59 (27.1)*	*17/62 (27.4)*	1.000
Erectile function ***(IIEF question 3 ≥ about half the time) reported by patients 12 months after surgery***				
IIEF question 3 (≥ about half the time)[b]		*34/74 (46.0)*	*48/98 (49.5)*	0.759
Urinary continence (Pad-free) reported by patients 12 months after surgery				
Pad-free[c]		*65/81 (80.2)*	*89/124 (71.8)*	0.189
Urinary continence (Pad-free and leakage free) reported by patients 12 months after surgery				
Pad-free and leakage free[d]		*36/71 (50.7)*	*59/107 (55.1)*	0.646

Characteristic		Age 39–59 year	Age 60–74 year	P value
Urinary continence (Change of pad less than once per 24 hours) reported by patients 12 months after surgery				
Change of pad less than once per 24 hours[e]		*75/81 (92.6)*	*106/125 (84.8)*	**0.126**
Potent and Continent at 12 months[f] *Potent IIEF question 3* (≥ *about half the time*) + continent (*Change of pad less than once per 24 hours*)				
	Yes	*36/87 (41.4)*	*50/134 (37.3)*	0.574
	No	*51/87 (58.6)*	*84/134 (62.7)*	
Trifecta at 12 months[g]				
	Yes	*34/87 (39.1)*	*50/134 (37.3)*	0.887
	No	*53/87 (60.9)*	*84/134 (62.7)*	

[a] Patients with preoperative IIEF > 21 and bilateral nerve-sparing during RP

[b] Patients with preoperative IIEF Q3 (≥ about half the time) and bilateral nerve –sparing

[c] Patients with preoperative Pad-free continence and bilateral nerve-sparing

[d] Patients with preoperative Pad-free and leakage-free continence and bilateral nerve-sparing

[e] Patients with preoperative Change of pad less than once per 24 hours and bilateral nerve-sparing

[f] Patients preoperative potent (≥ *about half the time*) + continent (*Change of pad less than once per 24 hours*)

[g] BCR-free or No local recurrence or no RT + potent *(≥ about half the time) + continent* (*Change of pad less than once per 24 hours*) among preoperative potent and continent patients.