

OUTCOMES OF ROBOTIC-ASSISTED RADICAL PROSTATECTOMY FOR PATIENTS IN TWO EXTREME AGE-GROUPS (< 50 YEARS VS > 65 YEARS)

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Abstract

Background and aims. To assess the outcomes of robotic radical prostatectomy in two different age subgroups of pre-operatively potent patients: younger than 50 years and older than 65 years.

Methods. We included in the present study a number of 202 patients with prostate cancer divided into two groups: 99 patients older than 65 years (group 1) and 103 patients younger than 50 years (group 2).

Results. More than half of the younger patients were low-risk vs 57% of the older patients who were high-risk. Overall positive surgical margins rate was 21.2% in group 1 vs 12.1% in group 2. The early biochemical recurrence at 6 months after radical prostatectomy was 4% in group 1 vs 11.6% in group 2. The continence rate at 6 months was similar between the two groups and was not correlated with the patients' age ($p=0.72$), nerve-sparing ($p=0.3$ for group 1, $p=0.92$ for group 2) or pathological staging (overall $p=0.81$, $p=0.89$ in group 1 and $p=0.63$ in group 2). We observed a significantly higher rate of potency for patients in group 2 (91.5% vs 47.2%, $p<0.0001$). The most important factor associated with the regain of potency at 6 months after the procedure was the age of the patient ($p<0.0001$), independently of the type of nerve-sparing performed.

Conclusions. Age seems to be the most important predictor of the regain of potency after robotic radical prostatectomy. Patients should be counseled accordingly in order to have realistic expectations about the functional results after robotic-assisted surgery.

Keywords: prostate cancer, prostatectomy, robotic surgical procedures, erectile function

Background and aims

Robotic-assisted radical prostatectomy (RALP) is one of the surgical techniques that has evolved the most rapidly after the implementation of robotic systems worldwide. The possibility of a better visualization of the operative field, ensuring a more precise apical dissection, the

preservation of a longer urethral length and the possibility of performing nerve-sparing have made the robotic approach a potential new gold standard for radical prostatectomy [1]. The robotic radical prostatectomy has been validated as a safe and feasible technique for localized prostate cancer by demonstrating similar oncological outcomes [2] to the other two types of approach (open or laparoscopic), with a significant advantage in terms of 12-month continence and

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potency rates [3,4].

In order to standardize the reporting of the perioperative and long term results of radical prostatectomy, the concept of pentapecta was proposed by Patel et al [5]. Pentapecta assesses the positive surgical margins rate, the early complications, the PSA dynamics after the surgery, the continence and potency of the patient. The authors reported a rate of 70.8% of achievement of pentapecta in a group of more than 300 patients who underwent robotic radical prostatectomy.

Asimakopoulos et al. [6] compared the rate of pentapecta between laparoscopic and robotic radical prostatectomy in 227 patients who underwent bilateral nerve-sparing and concluded that the possibility of achieving pentapecta in these patients was rather low, irrespective of the type of approach (27.5% for LRP and 45.6% for RALP). The age of the patients was associated with pentapecta outcomes, especially in the LRP group, each additional year leading to a 6% reduction of the possibility of achieving pentapecta. For patients older than 65 years, the robotic approach demonstrated a higher probability of potency recovery after the surgery (OR 4.6, $p=0.02$). Although the robotic approach showed more favorable functional outcomes, the main parameter that led to pentapecta failure for both types of approach was potency.

The causes of erectile dysfunction after radical prostatectomy are not strictly linked to the injury of the neuro-vascular bundles, but include also vascular dysfunction (lack of response to vasodilatative stimulation or loss of veno-occlusive mechanism) and neurapraxia [7,8]. Several techniques have been developed in order to improve the surgical technique of nerve-sparing. Tewari et al. observed that by reducing the traction of the neuro-vascular bundle, a diminished ischemic nerve-injury can be ensured [9]. Furthermore, Patel et al. have showed that the placement of dehydrated human amnion/chorionic membrane over the neuro-vascular bundles has an anti-inflammatory effect and may accelerate the return of continence and potency after RALP [10]. The use of a laparoscopic Doppler ultrasound probe to identify the vascular flow within the bundles can improve the neuro-vascular bundles identification and potentially ensure greater nerve preservation [11].

The impact of nerve-sparing upon the potency outcomes after robotic radical prostatectomy is still controversial and there might be other factors that have additional influence upon this outcome.

The objective of our study was to assess the outcomes of robotic radical prostatectomy in two extreme age subgroups of pre-operatively potent patients: younger than 50 years and older than 65 years.

Methods

We included in the present study a number of 202 patients with localized and locally-advanced prostate

cancer divided into two groups: 99 patients were older than 65 years and underwent robotic radical prostatectomy in one department (group 1); 103 patients were younger than 50 years and underwent robotic radical prostatectomy in another department (group 2).

The clinical staging included digital rectal examination and multiparametric MRI, when available. All patients underwent bone scintigraphy according to the current recommendation of the European Association of Urology [12].

For robotic radical prostatectomy, both departments used the technique described by Patel [13], with transperitoneal approach and 6 trocars (4 for the robot and 2 for the assistant surgeon). Nerve-sparing was performed in accordance with the clinical staging and the patient's status of sexual activity. Pelvic lymph node dissection removed the internal and external iliac and obturator fossa lymph nodes, and was performed according to the indication of Memorial Sloan Kettering Center nomograms.

Biochemical recurrence was defined as a PSA above 0.2 ng/ml in patients with undetectable PSA at 1 month after surgery. Patients were considered continent when using 0-1 safety pad/day and potent if they presented erections sufficient for intercourse with or without PDE5 inhibitors.

The statistical analysis was performed using Medcalc v.12.4 (MedCalc Software bvba, Ostend, Belgium; <https://www.medcalc.org>). $P<0.05$ was considered statistically significant.

Results

The clinical characteristics of the patients in the two study groups are presented in Table I.

We observed that the mean PSA was significantly higher in group 1 in comparison with group 2, but the number of positive biopsy cores was similar.

There was a significant difference regarding the clinical staging of the patients: group 2 included 54.5% more cT1c patients, whereas group 1 included 43.5% more cT2c and cT3 patients, which shows that patients older than 65 years presented with a more advanced stage at diagnosis. Also, the predominant cGleason score in group 2 was 6 (3+3), in comparison with group 1 which included similar percentages of cGleason 6 and 7 (3+4). As a result, more than half of the younger patients that underwent surgery were low-risk, whereas 57% of the older patients were high-risk.

There was a significant difference of 48 minutes in terms of operative time, in favor of group 2. Nerve-sparing was performed in 74.8% of cases in group 2, in comparison with 51.8% of patients with non-nerve-sparing in group 1. Pelvic lymphadenectomy was performed in a similar number of cases in the two groups, but the lymph node yield was significantly higher in younger patients. The blood loss difference was minimal (50 ml), in favor of group 2 (Table II).

Table I. Clinical characteristics of the patients in the two study groups.

	Age > 65 years (Group 1)	Age < 50 years (Group 2)	P
Age (years)	68 (95% CI: 67-69)	48 (95% CI: 47-48)	-
PSA (ng/ml)	8.6 (95% CI: 7.99-9.6)	5.4(95% CI: 4.9-6.8)	0.0013
No of positive biopsy cores	3 (95% CI: 3-5)	4 (95% CI: 3-5)	0.16
No of total biopsy cores	12	12	-
cT			<0.0001
cT1c	14.6%	69.1%	
cT2a	14.6%	21.6%	
cT2b	18%	0	
cT2c	28.1%	4.1%	
cT3a	19.1%	5.2%	
cT3b	5.6%	0	
cGleason			0.0004
6(3+3)	34.8%	69.3%	
7(3+4)	38%	16.8%	
7(4+3)	17.4%	8.9%	
8	7.6%	3%	
9	2.2%	2%	
Primary cGleason			0.04
3	75%	87.1%	
4	25%	11.9%	
5		1%	
Secondary cGleason			0.0004
3	52.2%	79.2%	
4	43.5%	18.8%	
5	4.3%	2%	
D'Amico risk group			<0.0001
Low	17.2%	56%	
Intermediate	25.8%	33%	
High	57%	11%	

Table II. Intra-operative and pathological comparison between the two groups.

	Age > 65 years (Group 1)	Age < 50 years (Group 2)	P
Operative time (min)	258	210	<0.0001
Nerve-sparing			<0.0001
No	51.8%	4.9%	
Unilateral	25.9%	20.4%	
Bilateral	22.4%	74.8%	
Blood loss (ml)	250	200	0.001
Lymphadenectomy	48.5%	59.2%	0.2
Lymph node yield	9	13	<0.0001
pT			0.43
pT2a	6.1%	8.2%	
pT2b	5.1%	5.1%	
pT2c	46.9%	55.1%	
pT3a	28.6%	24.5%	
pT3b	13.3%	7.1%	
Localized disease	58.2%	68.4%	0.18
Upstaging	26%	25%	1
pGleason			0.003
6(3+3)	25.3%	38.8%	
7(3+4)	61.5%	32.7%	
7(4+3)	11%	18.4%	
8	1.1%	6.1%	
9	1.1%	4.1%	
Primary pGleason			0.02
3	86.8%	71.4%	
4	13.2%	27.6%	
5		1%	
Secondary pGleason			0.006
3	36.3%	57.1%	
4	62.6%	39.8%	
5	1.1%	3.1%	
Perineural invasion	66.7%	58.3%	0.27
Lympho-vascular invasion	3%	2.9%	0.71

The pathologic assessment revealed no significant difference between the two groups, with the majority of patients in pT2c and pT3a disease. The upstaging rate at final pathology from cT2 to pT3 was similar for both groups.

Overall positive surgical margins rate was 21.2% in group 1 vs 12.1% in group 2. We did not identify any significant difference related to the age group when assessing positive surgical margins in pT2 or pT3 disease, the type of nerve-sparing that was performed or positive surgical margins' localization. The only significant difference between the two groups regarding positive surgical margins was observed for pT3 patients who underwent bilateral nerve-sparing (22.2% in group 1 vs 10% in group 2), probably due to the understaging of the disease (Table III).

The early biochemical recurrence at 6 months after radical prostatectomy was 4% in group 1 vs 11.6% in group 2, but not statistically significant and did not correlate with

the presence of positive surgical margins ($p=0.64$ for group 1 and $p=0.77$ for group 2). The continence rate at 6 months was similar between the two groups. We did not find any significant correlation between the continence rate and age of the patients ($p=0.72$), nerve-sparing ($p=0.3$ for group 1, $p=0.92$ for group 2) or pathological staging (overall $p=0.81$, $p=0.89$ in group 1 and $p=0.63$ in group 2) (Table IV).

We observed a significantly higher rate of potency for patients in group 2 (91.5% vs 47.2%, $p<0.0001$), although not correlated with the nerve-sparing ($p=0.2$ for group 1 and $p=0.82$ for group 2). The most important factor associated with the regain of potency at 6 months after the procedure was the age of the patient ($p<0.0001$), independently of the type of nerve-sparing performed. For the cut-off age of 50 years, the age of the patient showed an AUC of 0.87 (95% CI: 0.8-0.92), sensitivity of 81%, specificity of 87%, $p<0.0001$ for the prediction of potency outcome after the surgery.

Table III. Positive surgical margins in the two study groups.

	Age > 65 years (Group 1)	Age < 50 years (Group 2)	P
R1			
pT2	21.2%	12.1%	0.12
pT3	17.5%	12.1%	0.55
Multiple	26.8%	12.9%	0.25
Bilateral NS	38.2%	10%	0.19
Unilateral NS	31.6%	12.3%	0.09
Non-NS	22.7%	9.5%	0.44
	18.2%	20%	0.61
R1 in pT2			
Base	30%	12.5%	0.75
Apex	60%	37.5%	0.63
Posterolateral	50%	50%	0.63
Bilateral NS	16.7%	13.5%	0.86
Unilateral NS	14.3%	7.7%	0.94
Non-NS	18.2%	0%	0.37
R1 in pT3			
Base	55.6%	50%	0.67
Apex	55.6%	50%	0.67
Posterolateral	44.4%	25%	0.96
Bilateral NS	22.2%	10%	0.04
Unilateral NS	25%	14.3%	0.66
Non-NS	20%	25%	0.68

Table IV. Oncological and functional outcomes in the two study groups.

	Age > 65 years (Group 1)	Age < 50 years (Group 2)	P
Biochemical recurrence at 6 months	4%	11.6%	0.23
Continence at 6 months	90.7%	93.9%	0.72
Potency at 6 months	47.2%	91.5%	<0.0001

Discussion

A relatively small number of studies have compared so far the outcomes of RALP in elderly and young patients. Labanaris et al analyzed a cohort of 2000 patients (45 patients older than 75 years) and have concluded that RALP is a safe procedure for patients over 75 years and ensures good outcomes in selected older men with a life expectancy of more than 10 years [14]. Other authors observed a delay in the return of continence and lower potency outcomes in the elderly population [15,16]. Age has been repeatedly shown to be an independent predictor of post-operative erectile function, possibly as a result of an improved baseline sexual function [17].

In the present study, we observed that young patients that undergo robotic radical prostatectomy have low pre-operative PSA. Also, the urologists seem to be more aggressive with the disease in young patients, as they recommend the surgical procedure upfront for patients with clinical stage T1c or T2a, and low Gleason score. The majority of the young patients that underwent RALP met the criteria for low and intermediate risk groups and nerve-sparing procedure was performed in the majority of the cases. Pelvic lymph node dissection tends to be performed more thoroughly in young patients, so the lymph node yield was higher.

What was interesting to observe was that, although young patients seemed to be in lower T stages pre-operatively, the pathological examination revealed rather similar staging, irrespective of the age group, as Samadi et al. [17] also observed. As one would expect in this case, the rate of positive surgical margins in patients with pT3 stage that underwent bilateral nerve-sparing was higher in young patients. Also, we observed higher rates of extreme Gleason score 8 and 9 in younger patients, a surrogate for a more aggressive disease, similar to what has been reported in literature [18].

The present study assessed patients in two extreme age groups – < 50 years and > 65 years and the only significant difference we identified in terms of outcomes was the sexual function. Potency was regained at 6 months after the surgery in 91.5% of the young patients, in comparison with 47% of older patients, the age being significantly correlated with this outcome. Our reported rates of potency in young patients are higher than what has been published (69%), probably because of the high-volume centers.

Samadi et al. [17] published a study on a cohort of 2495 patients who underwent robotic radical prostatectomy and concluded that the cut-off age of 50 years can be used to predict faster and better recovery of potency than their older counterparts, age being an independent predictor for this outcome.

Mendiola et al. reported the outcomes of an age stratified group of 300 patients that underwent robotic radical prostatectomy. The authors observed that although

continence and potency were regained earlier by younger patients, one year after surgery the patients reported similar continence irrespective of the age group, while the difference regarding the potency was maintained [19].

Ludovico et al. analyzed 130 patients with a mean age of 68 years and observed that for this age group neither robotic approach, or retropubic approach for bilateral nerve-sparing radical prostatectomy influence the recovery of potency after the surgery [20]. On the other hand, some authors observed the superiority of RALP over the open technique for the regain of erectile function [21]. As Novara et al. stated, probably the main factor that influences the success of the nerve-sparing technique and potency recovery is a thorough selection of the patients based on standardized criteria. The authors consider that the best candidates for bilateral nerve-sparing radical prostatectomy are patients younger than 65 years, with no comorbidities and good preoperative erectile function [22].

The impact of age upon the functional results of robotic radical prostatectomy seems to be more significant than the type of nerve-sparing performed, but this issue is still a matter of debate.

The limitation of the studies published so far, including the present one, is the lack of: a cut-off age/age-group, a standardized pre-operative erectile function analysis, a record of the type (unilateral/bilateral) and extent (interfascial/intrafascial) of nerve-sparing and a standardized evaluation of the post-operative erectile function. Gathering all this information can assist the selection of the patients that should undergo a nerve-sparing procedure, but can also help the patients have realistic expectations about the post-operative results.

Conclusion

Age seems to be the most important predictor of the regain of potency after robotic radical prostatectomy. Patients should be counseled accordingly in order to have realistic expectations about the functional results after robotic-assisted surgery.

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