

ORIGINAL ARTICLE

Robotic-assisted radical prostatectomy – the 5-year Romanian experience

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Summary

Purpose: Radical prostatectomy is the standard therapeutic approach for localized prostate cancer. After the implementation of robotic surgery in Romania, the indication extended progressively to locally advanced prostate cancer. Our objective was to evaluate the oncological and functional outcomes in patients undergoing robotic-assisted radical prostatectomy (RARP), 5 years after the first intervention in Romania.

Methods: Between November 2009 and July 2014, 207 RARPs were performed using the da Vinci SI Surgical System. Perioperative data were prospectively collected. The oncological and functional follow-up was up to 55 months (range 3-55).

Results: Patient stratification according to D'Amico risk categories was 16% low risk, 56.7% intermediate risk and 27.3% high risk. Median console time was 210 min (range 160-360). Median blood loss was 300 ml (range 50-1300), transfusion being required in 2.9% of the cases. Histopatho-

logical examinations showed pT3 in 40.8% of the cases, with a positive surgical margin rate of 21.1%, 13.6% for pT2, and 32.1% for pT3. Continence rate (0–1 daily safety pad) at 6, 12, 24 and 55 months was 88.3, 88.8, 90.1, and 93.7% respectively. Overall sexual function restoration rate at 6, 12, 24 and 55 months was 41.1, 44.4, 47.4 and 53%, respectively. Biochemical recurrence rate during follow-up was 6.9%.

Conclusions: RARP is a minimally invasive therapeutic approach for prostate cancer, with acceptable outcomes, even in countries such as Romania, where the detection rate for localized prostate cancer is lower compared to other European countries due to lack of national screening programs.

Key words: functional, oncologic, prostate cancer, radical prostatectomy, robotic-assisted

Introduction

Prostate cancer is the dominating malignancy in men over 50 years, representing the 2nd cause of cancer death [1]. Although surgical treatment is associated with increased morbidity (incontinence, erectile dysfunction), radical prostatectomy remains the standard treatment. Starting with 2001, RARP is being performed after the emergence of the da Vinci surgical system, so that today the robotic-assisted approach has replaced the open approach as the most common surgical method for radical prostatectomy in USA [2].

The robotic system has several advantages such as three-dimensional high definition image, up to 10x magnification, instruments with 7 degrees of freedom, physical tremor reduction and enhanced ergonomics for the main operator [3]. These improvements provide the operator with the so much needed higher surgical precision when working in small operative spaces such as the male pelvis.

A number of recently published meta-analyses reveals equivalent oncological outcomes for

the 3 types of approach (open, laparoscopic and robotic-assisted). In terms of functional outcomes, robotic-assisted surgery yielded a faster continence and erectile function recovery compared to the other methods [4,5].

The purpose of our study was to assess the evolution of oncological and functional outcomes over a period of 5 years in patients who underwent RARP in the single robotic center for urological surgery in Romania.

Methods

Between November 2009 and July 2014, 207 da Vinci SI RARP were performed at the Urology Department of the Cluj-Napoca Clinical Municipal Hospital. All patients had pathologically confirmed prostate cancer (as shown by a standard 12-core prostate biopsy), in both localized and locally-advanced stages and any of the D'Amico risk groups. With prior informed consent of the patients, clinical data were recorded during the hospital stay, including perioperative parameters, as well as histopathological results. All patient data were collected prospectively. We included all consecutive cases upon receiving the patient informed consent. Of the 207 patients who underwent RARP, 9 were salvage prostatectomies (7 after high intensity focused ultrasound (HIFU), and 2 after cryotherapy).

Preoperative parameters included PSA, Gleason score after biopsy, positive biopsy rate and disease location, clinical disease stage as assessed by digital rectal examination, endorectal ultrasound, CT or multiparametric MRI, lower urinary tract symptomatology (International Prostate Symptom Score/IPSS survey form) and sexual function status (International Index of Erectile Function/IIIEF survey form).

The surgical technique used was first described by Patel [6], and interventions were carried out by three surgeons – one experienced senior surgeon and two surgeons in training. Standard pelvic lymph node dissection (obturator, internal and external iliac) was performed in all patients with a lymph node metastasis risk of 5% or higher according to Partin nomograms.

Intraoperative parameters were assessed and included console time (min), type of nerve-sparing (bilateral / one sided / none), lymphadenectomy status as well as blood loss (ml).

Histopathological examination results were recorded in the database with emphasis on the pTNM staging, histological type, Gleason score, positive surgical margin, tumor tissue volume and prostate volume, lymphovascular invasion, perineural invasion, number of excised lymph nodes and metastatic lymph nodes.

During follow-up we assessed PSA, continence and sexual function at 1, 3, 6 and 12 months in the first year after prostatectomy, followed by once every 6 months up to 5 years. Continence status was defined by the

number of daily urinary pads used (0, 1 safety pad, 2, 3, 4 and >4). Continence was defined as using none or a maximum of 1 daily safety pad. Sexual function was evaluated by asking the patients: “Do you get erections in the morning or after sexual stimulation?”, and in case of positive answer “Are your erections firm enough for intercourse?”. Careful monitoring was conducted in patients with neurovascular bundle preservation. Oncological outcomes were assessed by tracking the postoperative PSA dynamics in correlation with the surgical margin status. Biochemical recurrence was considered an increase in PSA over 0.2 ng/ml in patients with a first postoperative PSA lower than 0.1ng/ml.

Statistics

The clinical database was created using Microsoft Excel and the statistical analysis was performed using MedCalc v.12.4. Descriptive statistics were used for the overall results (mean and standard deviation or median with 95% confidence intervals, depending on data distribution) and χ^2 test for categorical variables. A p value <0.05 was considered statistically significant. For each parameter evaluated, cases were not considered where the required data was not available.

Results

The mean patient age at the time of RARP was 62.4 ± 5.88 years, with a mean body mass index (BMI) of 27.17 ± 3.23 kg/m². Median PSA value at the time of diagnosis was 8.35 ng/ml (95% CI 7.83-9.0), with a median prostate volume (as measured by endorectal coil MRI, endorectal ultrasound or CT) of 36.9 ml (95% CI 34.2-42.4). Clinical data, histopathological results and group risk stratification according to D'Amico criteria are presented in Table 1.

The median console time was 210 min (95% CI 200-224). Median blood loss was 300 ml (95% CI 250-350 ml). Blood transfusions were required in 6 patients (2.9%). There was 1 case in which open reintervention for hemostasis was required (bleeding source was the right neurovascular bundle). The mean time to catheter removal upon normal control cystography was 7 days. Bilateral nerve-sparing was performed in 37.2% of the cases, one-sided in 26.2%, and none in 36.6% of the patients. Pelvic lymph node dissection was performed in 99 cases (47.8%) with a positive rate of 9% (Table 2). There were no conversions to either laparoscopic or open surgery. Rectal wall lesions were registered in one patient (BMI=18 kg/m²) and intraoperative correction was promptly applied, with favorable evolution and with no intestinal bypass being required. There were no perioperative deaths.

Table 1. Perioperative clinical data and staging

<i>Clinical data</i>		
<i>Variable</i>	<i>Median</i>	<i>Range</i>
Age (years)	62.4	46–76
Body mass index (kg/m ²)	27.17	26.8–27.7
Preoperative PSA (ng/ml)	8.35	1–55.4
Prostate volume (ml)	36.9	16–121
Positive core biopsy number	4	1–12
IPSS	6	0–35
<i>Biopsy Gleason score</i>		
	<i>Biopsy Gleason score</i>	<i>Rate (%)</i>
	6	37.90
	7	56.50
	8	4
	9	1.50
<i>Clinical TNM stage</i>		
<i>TNM stage</i>	<i>Number of cases</i>	<i>%</i>
cT1c	32	15.50
cT2a	42	20.30
cT2b	48	23.20
cT2c	37	17.90
cT3a	35	16.90
cT3b	4	2
cX	9	4.20
<i>D'Amico risk groups</i>		
<i>TNM stage</i>	<i>Number of cases</i>	<i>%</i>
Low risk	31	16
Intermediate risk	110	56.70
High risk	53	27.30

BMI: body mass index, PSA: prostatic specific antigen, IPSS: international prostate symptoms score, cX: salvage therapy

Extracapsular invasion (pT3) was found in 40.8% of the cases and a Gleason score 7 in 74.6% of all patients. Overall rate of positive surgical margins was 21.1%, out of which 13.6% in pT2 and 32.1% in pT3. In 64.7% of the cases there was a single margin perforation, where multiple perforations were present in 35.5% of the patients. Apex tumors were found in 38.13% of the cases, basal in 30.5%, 14.4% posterior and 10.16% anterior and lateral, respectively. No positive margins were registered in pT2a-b cases (Table 3).

Progressive recovery rate of continence (0-1 daily pads) during follow-up was 53.4, 88.3, 88.8, 90.1 and 93.7% at 1, 6, 12, 24 and 55 months, re-

Table 2. Intraoperative parameters

<i>Intraoperative parameters</i>		
<i>Variables</i>	<i>Mean</i>	<i>Range</i>
Console time (min)	210	130 – 300
Laparotomy (conversion) rate	0	NA*
Blood loss (ml)	300	50 – 1300
Blood transfusion (cases)	6	
Catheterization time (days)	7	
<i>Nerve sparing</i>	<i>Number of cases</i>	<i>%</i>
Bilateral	77	37.20
One-sided	54	26.20
None	76	36.60
<i>Lymph node dissection %</i>		
Performed	99	48
Lymph node involvement	9	9

*NA: not available (no conversion cases)

spectively. The rate of patients with moderate preoperative symptoms (IPSS=8-9) improved significantly from 52.95 to 24.4% .

Erections were present in 83.5% of the patients prior to RARP. Postoperative sexual function scores during follow-up were 25.9, 41.1, 44.4, 47.4 and 53% at 1, 6, 12, 24 and 55 months, respectively (Table 4).

Out of the 207 cases of RARP, 19 (9.2%) had a PSA value >0.1 ng/dl 1 month after surgery. Biochemical recurrence (PSA >0.2 ng/ml) was encountered in 13 (6.9%) cases during follow-up.

Discussion

In Romania, there was an increase in locally advanced and metastatic disease at the time of diagnosis due to the lack of screening programs for prostate cancer. In the last 10 years, a screening program for prostate cancer was initiated in Cluj-Napoca [7], which is responsible for an increase in the diagnosis of localised disease, from 5 to 55%. This promoted the employment of radical prostatectomy as the standard treatment for localised prostate cancer which, starting with 2009, benefited further from the acquisition of a da Vinci surgical platform. However, the results of this study were influenced by a still high rate of locally advanced disease (Table 4).

In Canada, Zorn et al. [8] assessed the outcomes in 722 patients after RARP and found localised disease in 70.1% of the cases, compared to

Table 3. Histopathological results

Gleason score	Number of cases	%	
6	48	24.40	
7	147	74.60	
8	2	1	
Stage	Number of cases	%	PSM (%)
pT2a	18	9	0
pT2b	12	6	0
pT2c	89	44.30	18.20
pT3a	54	26.90	27.80
pT3b	28	13.90	40.70
Positive surgical margins	Number of cases	%	
Overall rate	42	21.10	
pT2	16	13.60	
pT3	26	32.10	
D'Amico risk groups			
TNM stage	Number of cases	%	
Low-risk	31	16	
Intermediar risk	110	56.70	
High risk	53	27.30	

PSM: positive surgical margins

59.2% in our patients, a characteristic that might explain the 210 min mean operative time and a mean blood loss of 300 ml compared to the Canadian study that had a mean operative time of

178 min and a mean blood loss of 200 ml. Also, we found an increase in the blood transfusion requirement rate (2.9%) vs 0.7% in Canadian study, but a comparable mean time to catheter removal of 7 days.

Concerning the oncological outcomes, our overall positive margin rate was 21.1% which is noticeably better compared to Ficarra et al. (29.5%) [9] and Zorn et al. (26.3%) [8], but, however, inferior to the 10.5% obtained by Patel et al. [6] (Table 5).

In defining continence we considered a patient continent when he used none or no more than 1 daily safety pad. Moore et al. reported a continence rate of 57% at 3 months and 85% at 12 months after radical prostatectomy [10]. We found that continence rates are comparable with the literature, even when considering a stricter definition (no daily pads). Novara et al. found a continence rate of 90% in 308 patients at 12 months [11] and Patel et al. reported a continence rate of 78 and 98% at 3 and 12 months, respectively [6]. Zorn et al. observed a continence rate of 79.9% at 6 months, which increased to 90.4% at 12 months after RARP [8].

The postoperative erectile function is also an important aspect despite a certain tendency of the patients to minimize its importance most probably due to the psychological impact of the diagnosis of malignancy. The same tendency was also observed in our study and we believe that this made the assessment of the sexuality parameters

Table 4. Functional outcomes

Urinary continence after RALP	Follow-up (months)		%	
	1	6		
			53.40	
			88.30	
			88.80	
			90.10	
			93.70	
IPSS	Before RARP (%)		After RARP (%)	
	1-7	44.10		74.40
	8-19	52.90	24.40	
	20-35	2.90	1.20	
Erectile function after RARP	Follow-up (months)	%		
		(overall)	(one-sided NS)	(bilateral NS)
	1	25.90	30.80	39.30
	6	41.10	32.00	45
	12	44.40	33	49.30
	24	47.40	37.40	61.50
	55	53.00	50.00	66.60

RARP: robotic-assisted laparoscopic radical prostatectomy, IPSS: international prostate symptom score, NS: nerve sparing

Table 5. Studies on functional and oncological outcomes in open, laparoscopic and RARP

First author [Ref no.]	Type	N	Mean follow-up (months)	Clinical data		
				PSM rate (%) (overall/pT2/pT3)	Potency at 1 year (%)	Continence at 1 year (%)
Rabbani [13]	RRP	225	12	NA	42	NA
Schover [14]	RRP	240	52	NA	NA	NA
Guillonneau [15]	LRP	550	36	16.7 / 11.9 / 36.7	66	82
Hoznek [16]	LRP	134	12	25 / 16.8 / 48.8	5.6	86
Rlassweiler [12]	LRP	438	12	22 / 7 / 35.4	NA	90
Hara [17]	LRP/RRP	52	6	NA	NA	NA
Patel [10]	RARP	200	9.7	10.5 / 5.7 / 28.5	NA	98
Bentas [18]	RARP	40	15	30 / 8.0 / 67	22	NA
Menon [9]	RARP	200	7.9	6 / 3 / NA	68	90
Tewari [19]	RARP	530	12	9 / NA / NA	78	98
Kaul [20]	RARP	154	12	6.4 / 4.6 / NA	96	97
Zorn [21]	RARP	722	18	26.3 / 18.3 / 46	52.4	90.4
Present study	RARP	207	18	21.1 / 13.6 / 32.1	44.4	88.8

RRP: radical retropubic prostatectomy, LRP: laparoscopic radical prostatectomy, RARP: robotic-assisted laparoscopic radical prostatectomy, PSM: positive surgical margins, N: number of cases, NA: not available

more difficult.

The inclusion of PSA in the national screening programs resulted in an increased rate of early diagnosis of prostate cancer, which yielded a higher number of younger patients with more active sexual function. On this basis, our efforts were also directed towards the preservation of potency and improved quality of life of our patients.

However, considering that most of the patients had criteria that stratified them in the intermediate and high risk groups according to D'Amico, and that 40.8% presented with capsular invasion, bilateral neural bundle preservation was performed in 37.2% of patients, and 26.2% underwent one-sided nerve-sparing operation. The rate of potency in patients that were sexually active prior to surgery and underwent either form of nerve-sparing operation was 41.1, 44.4 and 47.45% at 6, 12 and 24 months, respectively. Results presented in the literature vary widely. Zorn et al. reported a restoration of sexual function of 37.2% at 6 months and 52.4% at 12 months after

RARP [8], while Coelho et al. reported weighted mean potency rates of 61.1, 71.2 and 94% at 6, 12 and 18 months [12]. Murphy et al. reported a potency rate of 62% at 12 months after RARP [13].

In order to further aid the restoration of sexual function, patients were advised to take 5-PDE inhibitors. However, due to the high price of these agents and the fact that in Romania their cost is not reimbursed, the compliance to therapy was rather low. Another aspect to be taken into consideration is the high rate of advanced disease that impeded the full preservation of neural bundles.

Conclusion

Robotic-assisted radical prostatectomy represents a minimally invasive treatment for prostate cancer, with fairly good results, including countries such as Romania, where there is a significant rate of diagnosis of locally advanced disease due to the lack of screening programs.

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