Robot-assisted radical prostatectomy is a safe procedure

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ABSTRACT

INTRODUCTION: We present our departmental experience with robot-assisted radical prostatectomy and describe complications and early results for the first 239 consecutive patients.

MATERIAL AND METHODS: A total of 239 patients were planned to undergo robot-assisted radical prostatectomy performed with a DaVinci robot. Final histopathology and pre- and perioperative parameters were registered. Furthermore, early and late complications were recorded according to the Clavien-Dindo classification.

RESULTS: Robot-assisted radical prostatectomy was completed in 232 patients (97.1%). The median duration of surgery decreased significantly from initially 4.6 h in the first quartile to 3.1 h in the last quartile ($p < 0.001$). Overall, the median perioperative blood loss was 300 ml (range: 25-1,000 ml). The median admission time was one day (range: 1-5 days), and the median duration of bladder catheterization was eight days (range: 6-149 days).

In total, 88 post-operative complications were observed in 73 patients (31.5%). A total of 70 complications appeared within 30 days of surgery, whereas 18 occurred later. Among the early complications, the majority (57.1%) were minor (Clavien-Dindo grade ≤ II); however, overall 2.6% suffered an early grade ≥ IIIb complication. Overall, the margin-positive rate was 29.3% decreasing from 43.1% in the first quartile to 24.7% in the last three quartiles ($p = 0.008$).

CONCLUSION: Robot-assisted laparoscopic radical prostatectomy is a safe procedure with minimal blood loss, short hospitalization and short time catheter time post-operatively.

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Open retro-pubic radical prostatectomy was introduced in Denmark in 1995 as an intended curative therapy for patients with clinically localised prostate cancer [1]. During the past decade, robot-assisted radical prostatectomy has emerged as a treatment option in several high-volume centres, and the procedure was introduced at our institution in 2009. The literature suggests that the technique is safe with a relatively low risk of complications [2] and that it may have advantages compared with open surgery in terms of improved peri-operative and functional outcomes without compromising cancer control [3]. However, a significantly lower blood loss during surgery is the only difference that clearly and repeatedly has been demonstrated to date [3].

We present our departmental experience with the technique and describe complications and early results from robot-assisted radical prostatectomy in our first 239 consecutive patients.

MATERIAL AND METHODS

Between January 2009 and August 2012, 239 patients were scheduled for robot-assisted radical prostatectomy in the Department of Urology, Rigshospitalet, Copenhagen, Denmark. Patient data have prospectively been collected in a database approved by the Danish Data Protection Agency (file #2006-41-6256). The median follow-up was 1.5 years (range 0.3–3.7 years).

The procedure was performed with a DaVinci version A5.0 robot (Intuitive Surgical Inc., Sunnyvale, CA, USA) as described by the Glickman Urological Institute [4]. Two surgeons performed all operations. Both were experienced in open radical prostatectomy and had received an introduction to the robotic system at the IRCAD laparoscopic training centre, Strasbourg. Surgeon A performed five operations under supervision before independently performing the operation. After assisting surgeon A for 45 operations, surgeon B performed single steps of the procedure during the next 25 operations before independently performing the procedure.

Patients with clinically localised prostate cancer and a life expectancy of more than ten years were candidates for robot-assisted radical prostatectomy. Initially, only physically fit patients with a body mass index (BMI) < 30 kg/m^2 and without previous major abdominal surgery were candidates. In addition, patients should have a clinical tumour (cT) category ≤ 2, prostate-specific antigen (PSA) < 10 ng/ml, Gleason score ≤ 3 + 4, and no palpable tumour at the base or a lobus tertius. As the surgeons gained more experience, the criteria for being offered robot-assisted surgery were modified; and from mid-2010, all patients have been considered candidates. Indications for nerve sparing surgery and additional preoperative evaluations have previously been described [5]. Patients were staged according to the UICC's tumour node metastasis (TNM) classification [6].

For all patients, the following pre- and perioperative variables were available: lower urinary tract symptoms, BMI, cT category, Gleason score, PSA, type of nerve sparing approach, whether lymphadenectomy was performed or not, and whether the procedure was converted into open surgery or not. The duration of sur-

ORIGINAL ARTICLE

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TABLE 1

Baseline characteristics and final histopathological outcome.

	n	%	Median (range)
Baseline characteristics (N = 239)			
Age, yrs			63 (40-73)
BMI, kg/m^2			26 (19-33)
PSA, ng/ml			6.9 (1.7-54)
LUTS			
Yes	97	40.6	
No	128	53.6	
Missing	14	5.9	
Clinical tumour category			
1c	149	62.3	
2a/b	60	25.1	
2c	30	12.6	
Biopsy Gleason score			
GNA	6	2.5	
3 + 3	116	48.5	
3 + 4	108	45.2	
4 + 3	8	3.3	
4 + 4	1	0.4	
Risk group[a]			
Low risk	60	25.1	
Intermediate risk	140	58.6	
High risk	39	16.3	
Type of operation			
Without nerve sparing	77	32.2	
Unilateral nerve sparing	74	31.0	
Bilateral nerve sparing	88	36.8	
Lymphadenectomy	25	10.4	
Final histopathological outcome (N = 232)			
Pathological tumour category			
pT0	2	0.9	
pT2	204	87.9	
pT3	26	11.2	
Specimen Gleason score			
≤ 3 + 3	72	31.0	
3 + 4	143	61.6	
4 + 3	13	5.6	
≥ 4 + 4	4	1.7	
Tumour volume, ml			3.4 (0.24-56.7)
Margin-positive			
pT2	52	25.5	
pT3	16	61.5	
Overall	68	29.3	
Lymph node status			
N+	3	1.3	
N-	22	9.5	
Nx	207	89.2	

BMI = body mass index; GNA = Gleason score not assigned; LUTS = lower urinary tract symptoms; N+ = lymph nodes with cancer cells; N- = lymph nodes without cancer cells; Nx = lymphadenectomy not performed; PSA = prostate-specific antigen.
a) According to the D'Amico classification [19].

TABLE 2

Complications.

	n	%	Days, median (range)
Baseline (N = 239)			
Converting into open surgery	7	2.9	
Due to surgical complications	4		
Due to insufficient CO_2 insufflations	2		
Due to robot malfunction	1		
Final outcome (N = 232)			
Post-operative admission			1 (1-5)
Catheter			8 (6-149)
Complication			
Patients	73	31.5	
< 30 days	70	30.2	
≥ 30 days	18	7.8	
Overall	88	37.9	
Clavien-Dindo early[a]			
I	25	10.8	
II	15	6.5	
IIIa	24	10.3	
IIIb	5	2.2	
IVa	1	0.4	
Clavien-Dindo late[b]			
I	0	–	
II	2	0.9	
IIIa	8	3.4	
IIIb	8	3.4	
IVa	0	–	
Readmission			
Patients	28	12.1	1.5 (1-14)
2nd readmission	4	1.7	4 (2-21)
3rd readmission	1	0.4	1
< 30 days	24	10.3	2 (1-14)
≥ 30 days	9	3.9	1.5 (1-21)
Overall	33	14.2	2 (1-21)

a) < 30 days following surgery; b) ≥ 30 days following surgery.

gery (from incision to suturing of the skin), the total time used in the operation theatre (from arrival until the patient left the room), duration of preparation and recovery (total time minus surgical time), blood loss during surgery, days of post-operative admission (from surgery to discharge), number of days with bladder catheterisation and final histopathology were recorded for patients in whom robot-assisted surgery was completed. The cohort was stratified into quartiles in order to describe changes in variables during the study period. Differences in duration of surgery, blood loss and margin-positive rate for the surgeons were analysed after excluding the first 30 operations for each surgeon. Peri- and post-operative complications and morbidity were reported according to the Clavien-Dindo classification [7] by thorough reviews of patient charts and were stratified as early (< 30 days) or late (≥ 30 days). This was performed by two of the authors and crosschecked. In cases of discrepancies, the charts were re-read and discussed until agreement was reached.

Data are reported as median (range) unless otherwise indicated. The χ^2-test was used to test for independence and the Mann-Whitney test was used to compare continuous data. Linear regression was used to analyse the association between BMI and both surgical duration and blood loss. $p < 0.05$ was considered statistically significant. Statistical analyses were performed with SPSS version 19 (SPSS Inc., Armonk, New York).

Trial registration: not relevant.

RESULTS

In total, 239 patients were referred for the procedure. Surgeon A performed the majority of the procedures (72.8%). Baseline characteristics are outlined in **Table 1**.

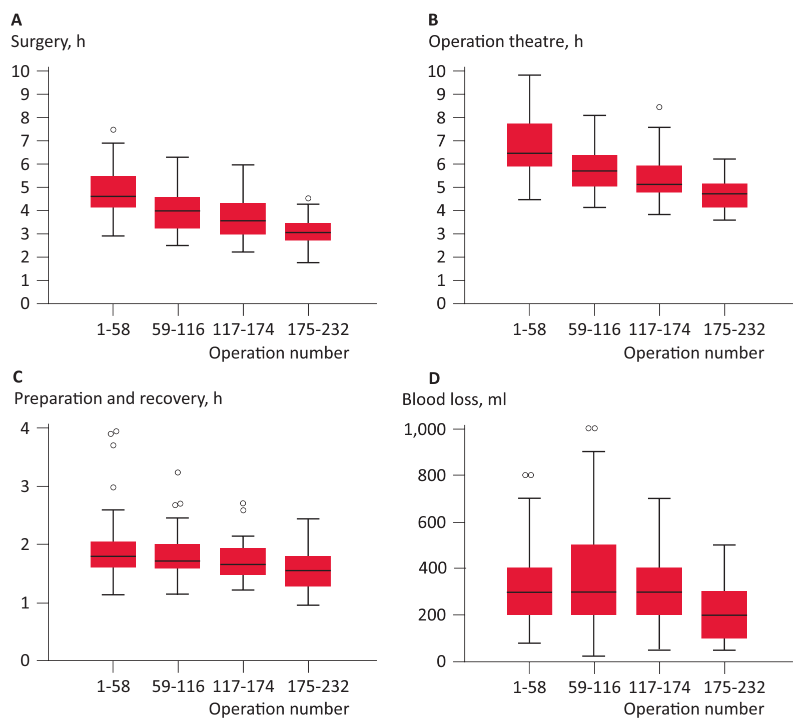
Of all radical prostatectomies performed at our institution, robot-assisted prostatectomies constituted 16.0% (42/263) in 2009, 19.9% (47/236) in 2010, 32.0% (77/241) in 2011 and 38.0% (73/192) in the first eight months of 2012. In 232 of the 239 patients (97.1%), robot-assisted radical prostatectomy was completed. Four patients were converted into open prostatectomy due to difficulties in identifying the boundaries of the prostate (patients number 9, 11, 12 and 103). The last three were converted during initiation due to insufficient CO_2 inflation (two patients) and a faulty robot arm (one patient).

The median duration of surgery decreased significantly from 4.6 h (2.9-7.5 h) in the first quartile to 3.1 h (1.8-4.6 h) in the last quartile ($p < 0.001$), **Figure 1**A. Also the median time used in the operating theatre and the duration of preparation and recovery decreased significantly, Figure 1B and Figure 1C. The perioperative blood loss was limited throughout the study period, with a median loss of 300 ml (25-1,000 ml). Nevertheless, it was significantly reduced over time ($p = 0.001$), Figure 1D. Four patients required blood transfusions.

There were no significant differences in mean duration of surgery between non-, uni-, and bilateral nerve-sparing approaches (4.0 h versus 3.9 h versus 3.9 h; $p = 0.66$) or between no lymphadenectomy and lymphadenectomy (3.9 h versus 4.1 h; $p = 0.20$). The association between increased BMI and an increase in surgical duration was not statistically significant ($\beta = 0.13$; 95% confidence interval (CI): –0.18-0.44; $p = 0.40$). The mean duration of surgery was lower for surgeon B than for surgeon A (3.9 h versus 3.0 h; $p < 0.001$). This most likely reflects differences in training. In terms of mean blood loss, a significant difference was found between no, uni-, and bilateral nerve-sparing approach (291 ml versus 294 ml versus 354 ml; $p = 0.04$) and between surgeon A and B (334 ml versus 237 ml; $p = 0.004$). Lymphadenectomy did not affect the mean blood loss (312 ml versus 338 ml; $p = 0.72$), nor was a higher BMI associated with increased blood loss ($\beta = 0.001$; 95% CI: 0.000-0.003; $p = 0.14$).

FIGURE 1

Patients stratified into quartiles according to operation number for: duration of surgery (**A**), time occupying the operation theatre (**B**), duration of preparation and recovery (**C**), and blood loss (**D**). Illustrated with box- and whisker plot. The data are shown as 25, 50, and 75 percentiles for each quartile, and minimum and maximum values are shown as whiskers. Outlier cases, defined as more than 1.5 times the interquartile range from the median, are marked with circles.



The median post-operative admission time was one day (1-5 days), and the median duration of bladder catheterisation was eight days (6-149 days). Four patients had a catheter inserted for more than three weeks. Three were due to leakage from the anastomosis and one was due to a complicated recovery following accidental perforation of the rectum.

In total, 88 post-operative complications in 73 (31.5%) patients were observed (**Table 2**). A total of 70 complications appeared within 30 days of surgery, whereas 18 were late. Of the early complications, the majority (57.1%) were minor (Clavien-Dindo grade ≤ II); however, of the total population, five patients (2.2%) suffered an early grade IIIb complication, and one patient (0.4%) had a life-threatening complication (multiple pulmonary emboli), **Table 3**. There was no difference in the incidence of early complications during the full study period ($p = 0.52$). The late complications were few, but the majority had a high Clavien-Dindo scoring.

In total, 28 patients (12.1%) were readmitted for a median duration of two days (1-21 days), Table 2. Three patients were readmitted two times and one patient three times. The majority (72.7%) occurred within 30

TABLE 3

Clavien-Dindo classifications.

	Grade	n (%)	Early/latea	Readmission, n (%)
Urologic complications				
Clot retention	I	7 (3.0)	7/0	
Catheter displacement[b]	IIIa	3 (1.3)	3/0	1 (0.4)
Urinary retention after catheter removal[b]	IIIa	11 (4.7)	11/0	7 (3.0)
Urethra obstruction				
Dilatation in outpatient clinic	IIIa	3 (1.3)	0/3	
Meatal stenosis	IIIa	1 (0.4)	0/1	
Sachse urethrotomy	IIIb	3 (1.3)	0/3	3 (1.3)
Polyuria	I	2 (0.9)	2/0	
Severe urinary incontinence; ProAct	IIIb	2 (0.9)	0/2	2 (0.9)
JJ-stent due to hydronephrosis	IIIb	1 (0.4)	0/1	1 (0.4)
Peroperative JJ-stent due to proximity to ureteral orifice	IIIb	1 (0.4)	1/0	
Anastomotic leakage				
Requiring prolonged catheter or intravenous antibiotics	II	2 (0.9)	2/0	2 (0.9)
Abscess	IIIa	1 (0.4)	1/0	1 (0.4)
Requiring drainage	IIIa	2 (0.9)	2/0	2 (0.9)
Other complications requiring flex cystoscopy	IIIa	5 (2.2)	1/4	1 (0.4)
Bowel complication				
Bowel or epigastrial pain	I	4 (1.7)	4/0	4 (1.7)
Rectal injury requiring iliostomy	IIIb	1 (0.4)	1/0	1 (0.4)
Intraoperative neurological complications				
Upper extremity	I	10 (4.3)	10/0	
Lower extremity	I	2 (0.9)	2/0	
Vascular complication				
Transfusion	II	4 (1.7)	4/0	
Wound haematoma	IIIa	3 (1.3)	3/0	
Bleeding requiring extra drainage	IIIa	1 (0.4)	1/0	
Haemorrhage requiring reoperation	IIIb	s3 (1.3)	3/0	
Lung embolus	IVa	1 (0.4)	1/0	1 (0.4)
Infections (treated conservatively)				
Urinary tract infection	II	3 (1.3)	2/1	
Epididymitis	II	1 (0.4)	0/1	
Wound infection	II	3 (1.3)	3/0	2 (0.9)
Other requiring readmission	II	2 (0.9)	2/0	2 (0.9)
Other				
Low blood pressure post-operative	II	2 (0.9)	2/0	
Tooth injury during intubation	IIIa	1 (0.4)	1/0	
Lymphocele needing drainage	IIIa	1 (0.4)	1/0	1 (0.4)
Hernia	IIIb	2 (0.9)	0/2	2 (0.9)

a) Early: < 30 days following surgery late: ≥ 30 days following surgery.
b) Early post-operative re-catheterizations were performed with flex cystoscopy resulting in Clavien-Dindo grade IIIa.

days of surgery. The reasons for readmission are listed in Table 3.

Overall, the margin positive rate was 29.3%, Table 1. In the first quartile, the margin-positive rate was 43.1% compared with 24.7% in the last three quartiles ($p = 0.008$).

No difference in margin-positive rate was observed between surgeon A (27.7%; 95% CI: 20.2-35.2%) and surgeon B (22.9%; 95% CI: 8.9-36.8%; $p = 0.56$).

DISCUSSION

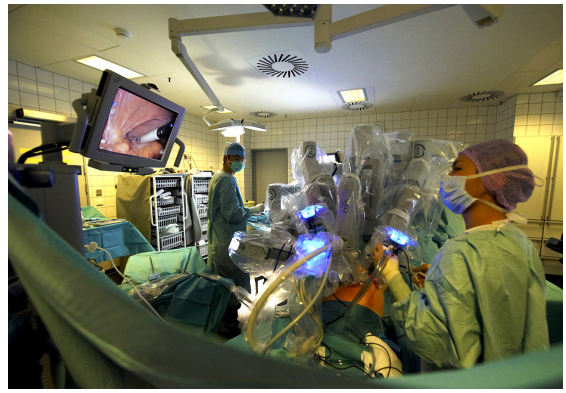
Since the introduction of robot-assisted radical prostatectomy, the technique has gained popularity around the world and currently almost 40% of all radical prostatectomies at our institution are robot-assisted. A minimally invasive surgical approach to localised prostate cancer was introduced in an attempt to minimise the morbidity associated with radical prostatectomy without compromising cancer control [8]. However, the shift from open to robot-assisted surgery has not been evidence-based. The DaVinci robot offers three-dimensional vision, seven degrees of freedom, and magnification, which intuitively seem to provide an optimal basis for more accurate dissection. On the other hand, the absence of the tactile dimension is often argued as a drawback.

In a recent review of robot-assisted radical prostatectomy, the mean duration of surgery was reported as 2.5 h (1.5-4.9 h), the mean blood loss was 166 ml (69-534 ml) and the mean catheterisation time was 6.3 days (5-8.6 days) [2]. The majority of the included studies were from high-volume centres. Nonetheless, our data on these parameters seem comparable.

The number of early complications ≥ grade IIIb in our series was 2.6% and this compares well with the literature (2.9-3.3% [9, 10]). However, the *overall* number of early complications was higher among our patients (30.2 versus 23.0-26.2% [9, 10]), which may reflect a lack of routine although differences in surveillance and recording of minor events most likely play a role when comparing between institutions.

The patients included in the present series represent a highly selected group and a comparison of complications to those encountered in patients undergoing an open procedure during the same time period was not attempted. However, our group has previously published data on peri- and post-operative complications in patients undergoing open radical prostatectomy [11]. In accordance with a recent review, robot-assisted surgery seems to lower peri-operative bleeding and shorten the duration of post-operative hospitalization [3].

Much of the literature on robot-assisted surgery originates from high-volume centres, and is typically based on one-man experiences. Margin-positive rates in these series are typically around 15% (6.5-32%) [12]. Our rate of 29.3% is of obvious concern. Still, it reflects a "real life" situation, when an institution, even one specialized in the management of prostate cancer, implements the robot-assisted technology. A recent study, more likely to represent "real life", is the PIVOT trial [13], where the margin-positive rates after a mix of open and robotic procedures were 17% and 31% for low risk and intermediate risk patients, respectively. Training and routine seem crucial, and it is likely that our margin-positive rate will continue to improve with more experience [14].



Robot-assisted radical prostatectomy.

Although surgeon A lacked prolonged early supervision which initially may have affected the margin-positive rate, we found no significant difference between the two surgeons after the first 30 operations. Moreover, the observed between-surgeon difference in duration of surgery and blood loss may at least to some extent be explained by confounders not accounted for in our statistics. Still, our results emphasize the importance of a meticulous, well-planned, and supervised training period. Rigorous training programmes and centralisation of the procedure to secure a high patient volume for the individual surgeon seems crucial in this type of surgery. Another argument for centralisation is the need to maintain expertise in open procedure, as conversions, although increasingly rare, will occur.

So where do we go from here? The answer is: we do not know [15]. There is yet no conclusive evidence to claim superiority of robot-assisted radical prostatectomy over the open procedure when it comes to cancer control or functional outcome. Basically, from a surgical anatomical point of view, the two procedures are very similar although they are performed with different tools. It therefore seems unlikely that meaningful differences in oncological outcome exist. The often heard need for a randomised trial comparing the two procedures is not easily met, as any potential differences between the two approaches will most likely be dwarfed by differences in individual surgical skills and experience with the given procedure [16]. Moreover, as surgical innovations continue to evolve and tend to be rapidly adopted, it seems increasingly unlikely that we will ever see a completed traditional randomised study based on oncological endpoints. Nevertheless, these difficulties do not justify absence of proper evaluation of multiple other parameters, including cost, and a randomized design remains desirable. Although future studies may demonstrate robotically assisted technique to be associated with reduced surgical stress, the lower blood loss and shorter hospitalisation so far remains the only significant benefits. On the other hand, likely because of unrealistic expectations, patient satisfaction has been shown to be lower in patients undergoing robotic surgery and consequently more patients regret undergoing the procedure [17]. Whether the increased cost and use of resources associated with robotic surgery is justified [18] is a challenge not only for surgeons, but also for economists and politicians, as the scarcity and just distribution of healthcare resources is increasingly in focus.

CONCLUSION

Robot-assisted radical prostatectomy is a safe procedure with minimal operative blood loss, short hospitalisation, short-term need for catheterisation and few severe complications. After the introduction phase, the margin-positive rate seems comparable to that of open surgery. The need for meticulous and well-planned training in robotic surgery is emphasized.

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CONFLICTS OF INTEREST: Disclosure forms provided by the authors are available with the full text of this article at www.danmedj.dk.

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