Prospective evaluation of urinary incontinence, voiding symptoms and quality of life after open and robot-assisted laparoscopic radical prostatectomy.

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Abstract:	Objective: • To compare functional outcomes (urinary incontinence (UI), voiding symptoms and quality of life) after open (ORP) and robot-assisted radical prostatectomy (RARP). Patients and methods: • Between September 2009 and July 2011, 180 consecutive patients underwent radical prostatectomy (RP). We prospectively assessed functional outcomes of 116 (ORP) and 64 (RARP) patients during the first year of follow-up. • UI was measured preoperatively (3 days-24hpad test) and daily after RP until total continence (3 consecutive days of 0 gram) was achieved. Additionally, all patients were assessed before and at 1, 3, 6 and 12 months after RP on IPSS, King's Health Questionnaire (KHQ). • All patients received pelvic floor muscle training until continence was achieved. • Kaplan-Meier analyses and Cox regression with correction for covariates were used to compare time to continence. Mann-Whitney-U test was used to assess IPSS and KHQ.

Results:

• Patients in the RARP group had significantly lower D'Amico risk group allocation and underwent more nerve sparing RP. Other characteristics were comparable.

• RARP patients regained continence sooner than ORP patients (p=0.007). Following RARP, median time to continence (16 vs. 46 days, p=0.026) and median amount of first day UI (49 vs. 169 gram, p<0.01) were significantly less compared to ORP. After correction for all covariates statistical evidence remained (p=0.026, HR 1.568 (1.055-2.329). Additionally younger men, men with positive surgical margins and men without preoperative incontinence achieved continence sooner.

• Comparison of time to continence between groups with a sufficient number of patients (intermediate risk and/or bilateral nerve sparing) still yielded a faster return of continence after RARP, but the effect decreased in size and lacked statistical significance (HR>1.2, p>0.05).

• Only 6 patients (2 RARP, 4 ORP) still had UI after 1 year.

• Patients in the RARP group had significantly better IPSS scores at 1 (p=0.013) and 3 (p=0.038) months and scored better in almost all KHQ aspects.

Conclusion:

• In this prospective trial, patients treated with RARP tended to regain urinary continence sooner than patients after ORP. However in subgroup analyses statistical significance disappeared and effect size decreased dramatically, indicating that results must be interpreted with caution.

REVISION NOTES

Referee: 1
Comments to the authors
This is an interesting article. It is well written and to the point. The assessment of continence was of a very good level.
These are my comments :
1. Use RARP instead of RALP (Best Practices in Robot-assisted Radical Prostatectomy: Recommendations of the Pasadena Consensus Panel, Montorsi et al, Eur Urol, 8 June 2012, pages 368 - 381)

We follow the reviewer and changed RALP into RARP in the whole document.

2. Methods:
When you speak about "over 3000 open procedures" and "more than 400 laparoscopic procedures", does that mean radical prostatectomy? Also laparoscopic PE has nothing to do with robotics, so you don't emphasize the expertise of that surgeon in robotics.

When we started the study in September 2009, the first surgeon had performed over 3000 open radical prostatectomies, the second surgeon had performed over 700 open radical prostatectomies and over 50 robot-assisted radical prostatectomies, the third surgeon had performed over 250 laparoscopic procedures and over 150 robot-assisted radical prostatectomies.

We acknowledge the reviewer in his comment that laparoscopic experience has nothing to do with robotics, so we changed this number in the methods-section to 150 RARP. (line 40-42): *One surgeon performed over 3000 open surgeries (HVP), the second surgeon performed over 700 ORPs and over 50 RARPs and the third surgeon performed more than 150 RARPs.*

Results :
3. The catheter stay is quite long: why?

In our hospital, patients are discharged at day 5 or 6 with the catheter. In the initial laparoscopic and robot experience we tried to remove the catheter after a cystogram but we stopped doing this since quite a lot of patients then got catheterized again because of the presence of a radiological sinus at the level of the anastomosis. So now, in the sake of uniformity, all the radical prostatectomy patients go home with a catheter and get back around day 12 where the catheter is then removed without cystogram.

We explained this in the discussion section (line 207-209): *Catheter stay was rather long for both groups. Reason for this is that all radical prostatectomy patients go home with the catheter in situ around day 6 and return to the hospital around day 12 where the catheter is then removed without cystogram.*

4. Nine patients had a longer stay of catheter: how many RARP, how many ORP? It is wrong to keep them out of the analysis.

We acknowledge the reviewer in his remark and included the outliers in the analysis. However because the outliers caused a rather skewed distribution, we described the median for both groups: median ORP (11 days), median RARP (12 days). Mean for ORP and RARP without omitting the outliers were 13.06 days (SD: 9.22) after ORP and 16.25 days (SD: 11.91) after RARP (p= 0.004).

Of these nine patients, had 3 open surgery and had 6 robot surgery. We added this to the results section (line 104-106).
We changed the mean into the median number of catheter days after ORP and RARP in Table 1.

5. At page 9 : use conversion instead of reconversion.

We follow the reviewer and changed reconversion into conversion.

6. The converted patients : what are their results?

Only five patients underwent a conversion from robot to open surgery (mean operative time was 242 minutes (range: 220-270)). The mean duration of incontinence was 17.6 days (SD: 20.08) (median: 9.0), the mean incontinence on the first day after catheter withdrawal was 270.6 gram (SD: 520.46) (median 51.0), the catheter remained on average 11.6 days in situ (SD: 0.89), the average age was 59.85 (SD: 2.83).

We added this to the results section (line 152-155).

7. The conclusion could be that this study adds to the evidence that in modern prostatectomy, whether performed in open or robotically, the results in continence are excellent and better than historical data. These results also add to the evidence that early continence is significantly better in the robotic group.

We acknowledge the conclusion of the reviewer and as also suggested by another reviewer, we tempered and reformulated the conclusion into '*In conclusion, in this prospective trial patients after RARP tended to regain urinary continence sooner than patients after ORP (24hpad test). However in subgroup analyses statistical significance disappeared and effect size decreased dramatically, indicating that results must be interpreted with caution. However, additionally, analysis indicated significant better scores concerning voiding symptoms severity and quality of life after RARP.*'
We changed this in the discussion-section (line 254-258).
We also adjusted this in the abstract (conclusion-section).

Referee: 2
Comments to the authors
Dear Authors

I liked your study, especially the fact you used well validated tools for your outcomes assessments. I have a few minor points I would like to see addressed prior to publication:

1. The selection of who got open and who got robot surgery is unclear. Exact criteria for each should be specified.

Initially, we stated in the manuscript that patients could not be randomized on surgical approach, because choice of surgical technique depended on tumor characteristics (size of the tumor, PSA), choice of the patient and medical history. As requested by the reviewer, we specified the exact criteria.

In fact, most patients chose the surgical approach based on personal preferences for open/robot surgery or a specific surgeon. Only when the medical condition of the patient did not allow for one or the other technique, a patient had no choice in the surgical approach. Low risk patients where more often operated with the robot while about all high-risk patients (≥ cT3, PSA ≥ 20 and Gleason Score ≥ 8) went for open surgery because they needed to undergo an extended lymph node dissection.

We added this to the methods-section (line 33-39).

2. The difference in continence outcomes between groups may reflect different degrees of NS performed (surrogately shown by the PSM rate). This would explain why men with PSM were quicker to achieve continence. This should be explained in the Discussion.

We agree with the reviewer. Indeed, the difference in continence outcomes between open and robot surgery is partially due to the different degrees of nerve sparing performed. Note that according to remark 5 of reviewer 3, we also decided to omit surgical margins status from the analysis, as in fact surgical margins status at least

partially reflects outcome. Correction for the different patient characteristics and nerve sparing status remained.

Univariate analysis of nerve sparing status indicated that patients with a bilateral nerve sparing status achieved continence sooner than patients with non-nerve (p= 0.034, HR= 1.719 (1.041-2.837))/unilateral nerve sparing surgery (p= 0.122, HR= 1.289 (0.738-2.251)). (We have added the univariate analysis in table 2, as also requested by another reviewer; data of nerve sparing status are shown with nonnerve sparing surgery as reference category). This effect disappeared in the multivariate analysis.

We added to the discussion-section following sentence (line 243-246): *The literature is not unanimous concerning the predictive value of nerve sparing status in time to continence.*[Sacco 06, Gacci 11, Yang 11, Suardi 12] *In our study, the difference in continence outcomes between open and robot surgery is partially due to the different degrees of nerve sparing performed, but only in the univariate analysis.(see table 2)*

3. Since the groups are different at baseline, there is significant selection bias, and undoubtedly residual confounding in your study after adjustment, your conclusions are too strong and should be further tempered. I think your study suggests that continence outcomes might be better after robotic than open surgery, and certainly nothing more than that.

Both groups (ORP and RARP) indeed differ at baseline concerning D'Amico Risk Groups and nerve sparing status. All other baseline characteristics did not differ between open and robot surgery. However, we agree with the reviewer that this is a confounding factor.

For that reason we first of all corrected for all baseline characteristics, which still indicated a significant difference between both groups (p= 0.026, HR 1.568 (1.055-2.329)). However, since nerve sparing status and D' Amico risk group significantly differed between open and robot surgery, we performed further analysis on this. As obvious from Table 1, only the intermediate group and the bilateral nerve sparing group had a sufficient number of patients in each group (ORP, RARP) to make a meaningful comparison possible. These subgroup analyses still yielded a faster return of continence after robot surgery (HR≥1.2), but indeed the effect was decreased in size and lacked statistical significance (Table 3).

As suggested by the reviewer, we tempered our conclusion and rephrased following sentences 'In conclusion, in this prospective trial patients after RARP regained urinary continence sooner than patients after ORP (24hpad test). However results have to be interpreted with caution, since statistical significance disappeared in subgroup analyses. Additionally, voiding symptoms severity and quality of life were significantly better after RARP.' into *'In conclusion, in this prospective trial patients after RARP tended to regain urinary continence sooner than patients after ORP (24hpad test). However in subgroup analyses statistical significance disappeared and effect size decreased dramatically, indicating that results must be interpreted with caution. However, additionally, analysis indicated significant better scores concerning voiding symptoms severity and quality of life after RARP.'*

We changed this in the discussion-section (line 254-258).

We also adjusted this in the abstract (conclusion-section).

Referee: 3

Comments to the authors

The study is interesting and well performed.

1. Introduction: Lines 36-43 are more indicated in the discussion section. Please modify.

We modified this and moved following part to the discussion (line 198-203) 'Immediately after catheter removal, continence rate is reported to be 10-41% after ORP [3, 7] and between 13.1% and 68.9% after RARP [7-10]. Continence rates increase to 63-83% after ORP [11-14] and 70-95% after RARP at 3 months [11, 12, 14]. Six months after surgery continence rate is between 83-89.6% (ORP) [13-15] and 75-95% (RARP) [14, 15].Twelve months after surgery, 80-94% (ORP) [7, 9, 12-14, 16] and 89-97% (RARP) [2, 9, 12, 14, 16] of patients have regained continence.'

2. How many patients were screened for the inclusion in the study? In other words, what was the % of patients included in the study of those who were given the possibility to enter?
Two hundred sixty one patients were eligible for study inclusion and 68.9% agreed to participate.

3. When was the PFMT started after catheter removal? Are the authors able to indicate whether all the patients correctly underwent PFMT?

After the surgery, pelvic floor muscle training was started the day of catheter removal. Patients were instructed to perform 10 short contractions of 1 second with 5 seconds of rest in between and 10 long contractions of 10 seconds with 10 seconds of rest in between, 3 times per day in lying, sitting and standing position. Patients also had to fill in their bladder diary daily (drinking volumes, micturition volumes, urine loss accurate to 1 gram, activities that caused urine loss) until total continence was achieved. Patients came to the hospital once a week to discuss the bladder diary and to perform an individual guided exercise session with manual control at the perineum during the first 6 weeks (in agreement with our urologists no anal palpation was performed during the first 6 weeks after surgery) and with anal palpation or EMG-biofeedback control from 6 weeks after surgery. Further patients had to indicate in which functional situations they had the most urine loss, f.e. walking stairs, getting out/in the car and then the therapist gave advice and exercised on how to use the pelvic floor muscles to prevent urine loss in this particular situation. PFMT was continued until total continence was achieved. Due to this close follow-up, we are rather sure that patients performed their contractions correctly.

We added this to the methods section (line 48-50): After the surgery, the PFMT program *was started on the day of catheter removal and* consisted of exercises of the pelvic floor manually controlled by the therapist and supplied with EMG-biofeedback.

4. Were the IPSS and the KHQ administered before surgery to each patient? If yes, these data should be shown in table 1.

IPSS and KHQ were administered before surgery to each patient. There was no difference in IPSS-score or any domain of the KHQ between ORP and RARP before surgery.
We added these data to table 1.

5. It is to me surprising that SM status achieved such a strong effect on urinary continence recovery, while risk group was not. I would suggest the authors to rerun the analyses removing SM status to see whether the severity of disease is associated with continence recovery, that would be more sound.
We acknowledge the suggestion of the reviewer. As surgical margin status, indeed at least partially reflects outcome, it is in fact not correct to correct for surgical margins status. For that reason, we excluded surgical margins status from the cox regression. However, it did not change the main result.

Variables in the Equation

	B	SE	Wald	df	Sig.	Exp(B)	95,0% CI for Exp(B)	
							Lower	Upper
TypeOP	,420	,201	4,385	1	,036	1,522	1,027	2,255
Lft	-,416	,190	4,785	1	,029	,660	,454	,958
RISKGROU			,563	2	,755			
RISKGROU(1)	-,011	,254	,002	1	,966	,989	,602	1,627
RISKGROU(2)	,147	,293	,254	1	,615	1,159	,653	2,056
NS			1,116	2	,572			
NS(1)	,105	,306	,117	1	,732	1,110	,610	2,021
NS(2)	,310	,327	,900	1	,343	1,364	,718	2,589
@24hpreopTOT0	,527	,185	8,134	1	,004	1,694	1,179	2,433
BMIpreopint			1,112	2	,574			
BMIpreopint(1)	-,048	,186	,067	1	,796	,953	,663	1,371
BMIpreopint(2)	-,270	,263	1,055	1	,304	,763	,456	1,278

In addition (also to remark 6 of this reviewer), we have added the univariate analysis. (see Table 2) This revealed that in the univariate analysis, patients with bilateral nerve sparing status achieved continence sooner. Although not significant, we could also see a trend indicating that low risk groups tended to achieve continence sooner (intermediate versus low: p= 0.380 (HR: **0.810** (0.506-1.297), high versus low: p= 0.134 (HR: **0.686** (0.420-1.122)). From this analysis, it seems that the severity of disease is not independently related to continence recovery.

We changed this in table 2.

6. Tables 2 and 3 should also report the univariable analyses.

As also explained in remark 5, we added all univariable analyses in Table 2. In table 3, the first line (without correction for confounders) represents the univariate analysis.

7. The last paragraph of the results section could be omitted, since those results do not correspond to the aims of the study.

The first reviewer asked additional data on the converted patients, that are described in the last paragraph of the results section. However, we agree that the part concerning the operative time of both surgical techniques is beyond the scope of this study and we omitted these sentences (line 152-155).

The remaining part of the text is: *Five patients underwent a conversion from robot to open surgery. The mean duration of incontinence was 17.6 days (SD: 20.08) (median: 9.0), the mean incontinence on the first day after catheter withdrawal was 270.6 gram (SD: 520.46) (median 51.0), the catheter remained on average 11.6 days in situ (SD: 0.89), the average age was 59.85 (SD: 2.83).*
Data were analyzed following the intention to treat principle. Surgical margins rate did not significantly differ between the open and robot group, although raw data differ a lot (21% (ORP) versus 30% (RARP) positive/doubtful surgical margins) (Table 2). Additionally, there was no difference between both groups in apical surgical margins rate.

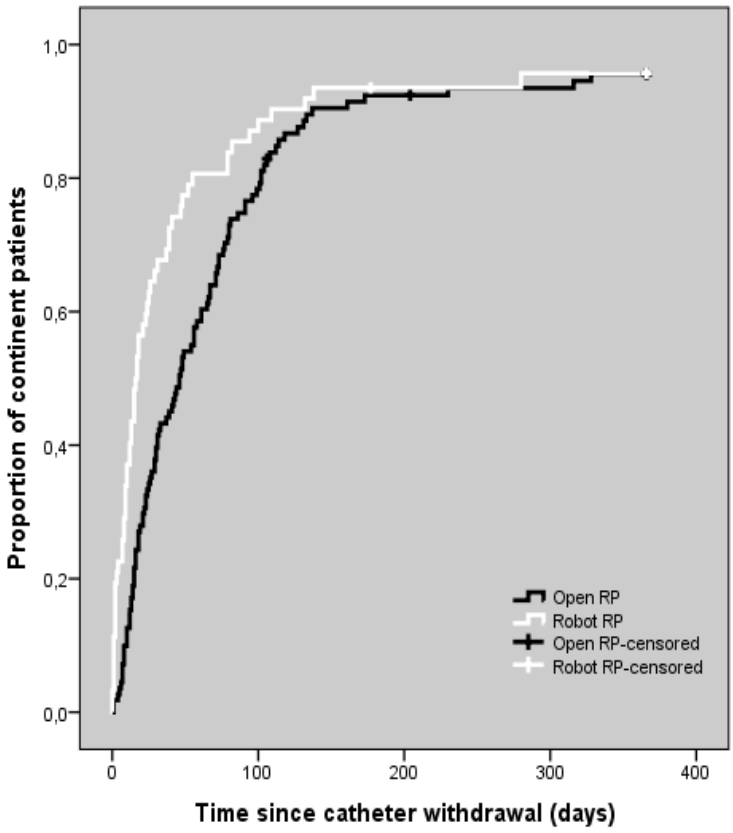
8. Table 3: it is not clear why the authors are showing the results of the subgroup analyses only in these select groups of patients (and none of them is significantly). They should try to show the results of subgroups analyses when they are significant!

As indicated in Table 1: nerve sparing status and D'Amico risk group significantly differ between ORP and RARP at baseline. All other baseline characteristics did not differ between open and robot surgery.

However, if we want to make a meaningful comparison between both groups, we can only do so, when a sufficient number of patients is included in each group. Since this is only the case for the intermediate risk group (50 patients (ORP) versus 43 patients (RARP)) and for the bilateral nerve sparing group (52 patients (ORP) versus 60 patients (RARP)), we only performed the subanalysis for this group of patients. (f.e. it would not be meaningful to compare 24 non-nerve sparing patients in the ORP group with 0 patients in the RARP group) These subgroup analyses still yielded a faster return of continence after robot surgery (HR≥1.2), but the effect was decreased in size and lacked statistical significance (Table 3).

9. Figure 1: I suggest the authors to run the KM analysis using the 1-KM method in order to obtain rising curves.

As requested by the reviewer, we reran the KM analysis to obtain rising curves. (See Figure 1)



Prospective evaluation of urinary incontinence, voiding symptoms and quality of life after open and robot-assisted radical prostatectomy.

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Keywords: urinary incontinence, voiding symptoms, quality of life, open and robot-assisted radical prostatectomy

Introduction

Since many years radical prostatectomy (RP) is the preferred therapeutic option for patients with localized or locally advanced prostate cancer [1]. Open radical prostatectomy (ORP) has been the most commonly used surgical technique for decades. Recently, robot-assisted radical prostatectomy (RARP) has become an equal alternative [2]. Despite the large number of radical prostatectomies performed, urinary incontinence (UI) remains a common postoperative sequel [3-6].

Several studies compared UI after ORP and RARP. Different studies found that patients achieved continence much earlier after RARP than after ORP [7-9], other studies could not confirm this [10-12]. The international prostate symptom score (IPSS) for evaluation of voiding symptoms was used in several studies [13-15]. IPSS scores ameliorated after surgery in all studies.

Miller et al compared health-related quality of life (HRQoL) between ORP and RARP in a small cohort of 162 patients [16]. They found a faster return to baseline HRQoL in patients after RARP. In contrast, Malcolm et al could not confirm these results [17]. Additionally Hara et al demonstrated that quality of life due to difficulty of urinary incontinence was significantly disturbed by surgery [18].

The objective of this study was to compare functional outcomes (UI, voiding symptoms and quality of life) of patients who underwent ORP versus RARP.

Methods

Patients

One hundred sixteen and 64 patients with localized or locally advanced prostate cancer and planned for ORP or RARP in the University Hospitals Leuven between September 2009 and July 2011, agreed to participate in this trial. All men signed a written informed consent. Exclusion criteria were: cognitive problems, non-Dutch speaking and simultaneously planned for a salvage procedure or other surgery in the pelvic region.

Procedure

Before surgery, patients were recruited on the outpatient clinic of urology. Patients could not be randomized on surgical approach, because most patients chose the surgical approach based on personal preferences for open/robot surgery or a specific surgeon. Only when the medical condition of the patient did not allow for one or the other technique, a patient had no choice in the surgical approach. Low risk patients where more often operated with the robot while about all high-risk patients (≥ cT3, PSA ≥ 20 and Gleason Score ≥ 8) went for open surgery because they needed to undergo an extended lymph node dissection. Three surgeons each specialized in ORP and/or RARP completed all operations. One surgeon performed over 3000 open surgeries (HVP), the second surgeon performed over 700 ORPs and over 50 RARPs and the third surgeon performed more than 150 RARPs. Open surgery for low/intermediate and high risk patients was performed according to the technique previously described [19, 20]. Robot surgery was performed as described by Menon et al [13].

Interventions

All patients followed individual pelvic floor muscle training (PFMT), on an outpatient basis once a week, until total continence was achieved. Continence was defined as three consecutive days of 0 gram urine loss using the 24hpad test. After surgery, the PFMT program was started on the day of

catheter removal and consisted of exercises of the pelvic floor manually controlled by the therapist and supplied with EMG-biofeedback. All patients were treated by a dedicated and specialized therapist. Additionally patients performed 60 contractions per day at home.

Assessments

All patients performed a 24hpad test during three days before surgery. After catheter withdrawal urine loss per 24 hours was daily recorded until continence was achieved. Auto-measurements of the patients were double-checked on a regular base by weighing the pad the patients wore, when they came to therapy. Furthermore, from time to time, patients were asked to collect all diapers from 24h in a plastic bag and take it to the hospital for an additional measurement. No difference was made in analyzing types of incontinence (stress, urge).

Furthermore all patients were prospectively assessed before and 1, 3, 6 and 12 months after surgery in the department of physiotherapy. Patients had to perform a 1hpad test, fill in a visual analogue scale (VAS) concerning their subjective feeling about urinary incontinence and fill in the international prostate symptom score (IPSS), a questionnaire to evaluate voiding symptoms (score 0-35). Additionally the King's health questionnaire (KHQ), a self-administered questionnaire designed to assess the impact of urinary incontinence on quality of life was completed. The nine domains of the questionnaire are general health perception, incontinence impact, role limitations, physical limitations, social limitations, personal relationships, emotions, sleep or energy and severity measures. Additionally weight and height were assessed. One well trained assessor performed the measurements. Urodynamic measurements were not performed in the first year after surgery. In the initial postoperative period no anticholinergics were prescribed.

Primary outcome parameters were time to continence and cumulative incidence of continence (24hpad test). Secondary outcomes were the point prevalence of continence, measured with the

1hpad test and the VAS at 1, 3, 6 and 12 months after surgery. At the same time points, IPSS and KHQ were assessed.

Statistical analysis

Patients' characteristics between the ORP and RARP group were compared. An independent *t*-test was used for continuous, normal distributed data and the Fisher's exact/ χ^2 test for categorical data.

Data were analysed according the intention to treat principle. Kaplan-Meier analyses with log rank test were used to compare the time to continence between both types of surgery. Drop outs were censored at moment of last follow-up. Afterwards a Cox regression was applied to compare the different groups concerning the time to continence with correction for the different covariates. Fisher's exact test was used to compare objective and subjective point prevalence's of urinary continence, defined as 0 gram on the 1hpad test and the VAS, measured at 1, 3, 6 and 12 months after surgery. For comparison of the voiding symptom severity and the health related quality of life at 1, 3, 6 and 12 months after surgery, the Mann-Whitney-U test was used, because the data were not normally distributed. All data were analyzed with SPSS 19.0.

The procedures of the study received ethical approval from the commission medical ethics of the University Hospitals Leuven responsible for human/animal experimentation (ML5470).

Results

One hundred sixteen and 64 patients underwent ORP and RARP, respectively. Seven patients were lost to follow-up immediately after surgery because of sudden death (n=1), cerebrovascular accident (n=1) or transport problems (n=5). Three other patients dropped out of the study at 106, 177 and 204 days after surgery with respectively 4, 17 and 28 gram of remaining incontinence (24hpad test). The indwelling catheter was removed after a median of 11 and 12 days after ORP and RARP respectively. Nine patients were classified as outliers (6-32-34-40-41-43-49-75 and 101 days of catheter wearing), but not omitted from analysis. Three had open surgery and six had robot surgery. Because randomization could not be performed on surgery level, D'Amico risk group and nerve sparing status differed between both types of surgery. All other baseline characteristics were comparable between ORP and RARP (Table 1).

Median time to continence was 46 days for patients after ORP and 16 days after RARP (p=0.026). The median amount of first day incontinence was 186 gram and 44 gram for the open and robot group, respectively (p<0.05).

Primary outcomes

Figure 1 demonstrates the Kaplan-Meier survival analysis for the time to urinary continence according to type of surgery (Figure 1). Patients after RARP achieved continence significantly faster than patients after ORP (p= 0.007). After correction for the different patient characteristics (age, D'Amico risk group, nerve sparing status, surgical margins status, preoperative urine loss, BMI) the statistical evidence remained (p= 0.026, HR 1.568 (1.055-2.329)) (Table 2). Additionally, age (p=0.04, HR 0.683 (0.470- 0.991), surgical margins status (p<0.001, HR 2.245 (1.518-3.320)) and preoperative urinary incontinence (p= 0.002, HR 1.794 (1.245-2.584)) were significant contributing factors, indicating that younger men, men with positive surgical margins and men without preoperative incontinence achieved continence sooner. However, nerve sparing status and D' Amico risk group

significantly differed between open and robot surgery (Table 1). Clearly, a comparison of the time to continence between open and robot surgery was only meaningful in the intermediate risk group and/or bilateral nerve sparing group, because only these groups had a sufficient number of patients. These subgroup analyses still yielded a faster return of continence after robot surgery (HR≥1.2), but the effect was decreased in size and lacked statistical significance (Table 3).

Four patients after ORP and two after RARP were not continent 12 months after surgery (Table 4). Compared to patients after ORP, significantly more RARP patients were continent at 1 month after surgery. Additionally, RARP patients had significantly less urine loss at 1 month postoperative.

Secondary outcomes

The point prevalence of continence, defined as 0 gram on the 1hpad test and the VAS, only significantly differed at 1 month after surgery (Table 5). Furthermore, the RARP group had significantly fewer voiding symptoms than the ORP group at 1 (p= 0.013) and 3 (p= 0.038) months after radical prostatectomy. At 1 month after surgery, the RARP group scored better in all aspects of the King's Health questionnaire, compared to the ORP group. Further 'sleep/energy' and 'severity measures' were significantly better after RARP at 3 months postoperative. At 12 months, patients after open surgery were more physically limited and took more precautions to avoid urine loss compared to patients after RARP (p= 0.014 and p= 0.011, respectively).

Fifteen patients (12.9%) after ORP and eight patients (12.5%) after RARP received additional radiotherapy. Radiotherapy was always started after continence was achieved, except in 3 patients. In these patients, mean urine loss was 7, 8 and 64 gram per 24 hours, respectively, at the start of additional radiotherapy. Thirty percent of patients had some preoperative urine loss (range 1-10 gram/day). These patients achieved continence significantly slower than preoperatively continent

patients (p= 0.01). Of the 6 patients, who remained incontinent one year after surgery, 3 patients had minimal urine loss preoperative (range 1-3 gram).

Five patients underwent a conversion from robot to open surgery. The mean duration of incontinence was 17.6 days (SD: 20.08) (median: 9.0), the mean incontinence on the first day after catheter withdrawal was 270.6 gram (SD: 520.46) (median 51.0), the catheter remained on average 11.6 days in situ (SD: 0.89), the average age was 59.85 (SD: 2.83).

Data were analyzed following the intention to treat principle. Surgical margins rate did not significantly differ between the open and robot group, although raw data differ a lot (21% (ORP) versus 30% (RARP) positive/doubtful surgical margins) (Table 2). Additionally, there was no difference between both groups in apical surgical margins rate.

Discussion

Patients after RARP regained urinary continence sooner than patients after ORP (24hpad test). The median time to continence and the median amount of UI on the first day after catheter removal were significantly less after RARP. This was further confirmed by the significant difference in the 1hpad test and VAS score at one month postoperative in favor of RARP. After correction for the different patient characteristics (Table 1) the statistical evidence in favor of RARP remained (p= 0.026, HR 1.568 (1.055-2.329)). Comparison of time to continence between ORP and RARP with a sufficient number of patients (intermediate risk and/or bilateral nerve sparing) still yielded a faster return of continence after RARP, but the effect decreased in size and lacked statistical significance. Additionally, voiding symptoms severity and quality of life were significantly better after RARP. Only six patients, four after ORP and two after RARP still had involuntary urine loss after one year (range 6-167 gram/day).

Our study had several strengths. First of all, this was a prospective study in which we studied the evolution of urinary incontinence, voiding symptoms and quality of life. Secondly, all of our patients were followed up for 12 months and evaluated at regular time intervals. Further all patients measured their urine loss daily during 24 hours by weighing their pads accurately to one gram. Additionally, patients performed a 1hpad test and a VAS concerning the subjective feeling of incontinence at regular time intervals (1, 3, 6 and 12 months postoperative). Patients were operated by three experienced surgeons, who used highly standardized surgical procedures. Further voiding symptoms and quality of life were assessed at 1, 3, 6 and 12 months after surgery. A limitation was that the number of patients in the open and robot surgery group was not equal (116 vs. 64 patients).

According to the literature, immediately after catheter removal, continence rate is reported to be 10-41% after ORP [3, 8] and between 13.1% and 68.9% after RARP [7, 8, 13, 21]. Continence rates increase to 63-83% after ORP [9, 10, 22, 23] and 70-95% after RARP at 3 months [9, 10, 22]. Six

months after surgery continence rate is between 83-89.6% (ORP) [9, 23, 24] and 75-95% (RARP) [9, 24]. At 12 months after surgery 80-94% after ORP and 89-97% after RARP has regained continence [8-11, 13, 23]. Our study achieved even better results with 96% continence after ORP and 97% after RARP. Only six patients remained incontinent one year after surgery. Four patients underwent a male sling procedure and were continent afterwards. Two patients refused incontinence surgery: one patient because of several other comorbidities (130gr) and the other patient because of minimal urine loss (6 gram). Catheter stay was rather long for both groups. Reason for this is that all radical prostatectomy patients go home with the catheter in situ around day 6 and return to the hospital around day 12 where the catheter is then removed without cystogram.

Contrary to several other studies [7-9] we used objective and subjective parameters to evaluate urine loss. In our study, patients performed a 24hpad test preoperatively (three days) and postoperatively daily until continence was achieved. Furthermore all patients performed a 1hpad test and filled in a VAS at fixed time-points. For the VAS, a score of 0 or 1 was interpreted as continent. Many patients scored themselves as 1 on the VAS, although they were completely dry using the 1h – and the 24hpad test. Usually, this was for safety reasons or because of post-micturition dribble less than 1 gram/ day.

Comparison of ORP and RARP demonstrated that the median time to continence decreased from 160 days to 44 days with RARP [7], but at 6 months no difference in continence rates could be found in two other matched comparison series [11, 22] In our study median time to continence was 46 days after ORP and 16 days after RARP. Similar to the studies of Krambeck et al and Ahlering et al, no differences in continence rates could be found at 6 months after surgery with 94% (ORP) and 95% (RARP) continence.

According to Namiki et al voiding symptoms, measured with the international prostate symptom score (IPSS) significantly improved after ORP [14]. Similarly Sammon et al and Menon et al indicated that voiding symptoms also ameliorated after RARP, but no level of significance was indicated [13,

15]. In our study IPSS ameliorated in both groups, but the RARP group performed significantly better in the short term (1 and 3 months after surgery) compared to the ORP group.

Comparing different studies concerning quality of life is difficult, because different questionnaires were used among studies. Miller et al compared quality of life during the first 6 weeks after ORP and RARP in a small cohort of 162 patients using the 12-item Short Form questionnaire (SF-12). They found better physical scores and a faster return to baseline health-related quality of life in patients after RARP [16]. Similar to Miller et al, we also found a faster return in quality of life in RARP patients. On the contrary, Malcolm et al (2010) could not find any pronounced advantages to RARP vs. ORP from the standpoint of HRQoL outcomes, using the UCLA-PCI questionnaire [17]. In our study, the King's Health Questionnaire was used, a questionnaire designed only to assess the impact of urinary incontinence on quality of life. Furthermore Hara et al found in a sub analysis, using the EORTC-prostate cancer-questionnaire, comparing patients before and after ORP, that quality of life due to voiding dysfunction was impaired before and significantly improved after ORP. In contrast, quality of life due to difficulty of urinary incontinence was significantly disturbed by surgery [18]. In our trial, patients after RARP had significantly fewer voiding symptoms compared to the ORP group at 1 and 3 months after surgery. Additionally patients after ORP took more precautions to avoid urine loss at 12 months postoperative. Differences between both surgical approaches were highest in the short term. This is normal because patients progress the most in the early postoperative period. The literature is not unanimous concerning the predictive value of nerve sparing status in time to continence [25-28]. In our study, the difference in continence outcomes between open and robot surgery is partially due to the different degrees of nerve sparing performed, but only in the univariate analysis.(see table 2) According to Ferronha et al, no substantial differences can be found between both surgical techniques regarding the positive margins [29]. Surgical margins rate did not significantly differ between the open and robot group, although raw data would suggest otherwise. Furthermore no difference between apical surgical margins rate was found, indicating that patients after robot

surgery were not better continent, because part of the apex was not removed and urethral sphincter was less damaged.

In conclusion, in this prospective trial patients after RARP tended to regain urinary continence sooner than patients after ORP (24hpad test). However in subgroup analyses statistical significance disappeared and effect size decreased dramatically, indicating that results must be interpreted with caution. However, additionally, analysis indicated significant better scores concerning voiding symptoms severity and quality of life after RARP.

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Figure 1: Time to urinary continence according to type of surgery

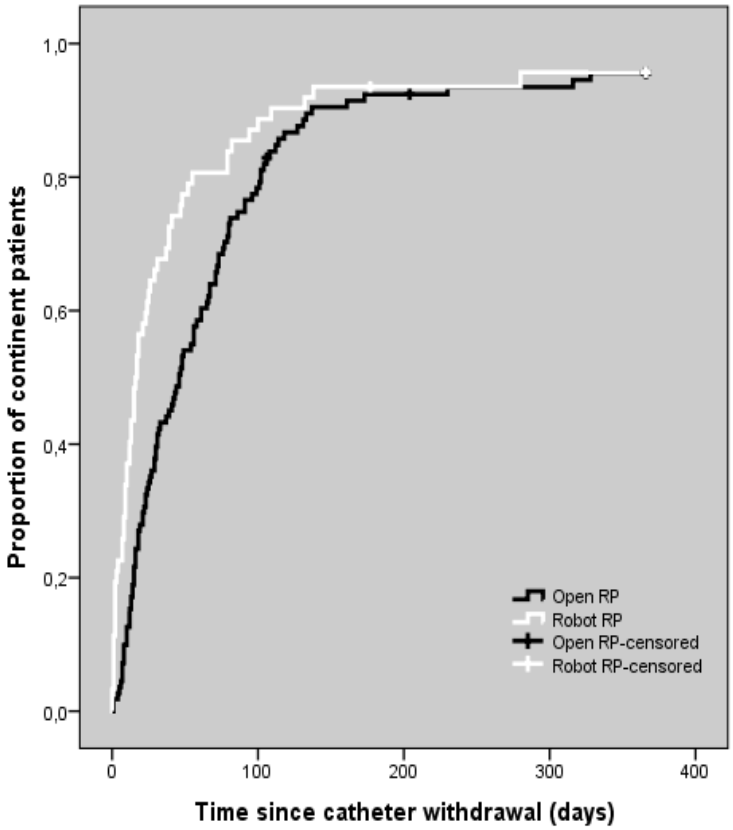

Table 1: Characteristics of patients according to type of surgery. Figures are numbers (percentages) of patients unless specified otherwise.

	ORP n= 116	**RARP** n= 64	**p-value**
Mean (SD) age (years)	62,22 (6,12)	61,48 (6,08)	0,436*
Median time urinary catheter (days)	11	12	0,252*
D'Amico Risk Group			**0,000****
I	8 (7)	14 (22)	
II	50 (43)	43 (67)	
III	57 (49)	7 (11)	
Missing	1 (1)	0 (0)	
Nerve sparing			**0,000****
Non-nerve sparing	24 (21)	0 (0)	
Unilateral-nerve sparing	40 (34)	4 (6)	
Bilateral-nerve sparing	52 (45)	60 (94)	
Missing	0 (0)	0 (0)	
Surgical Margin status			0,204**
Negative	91 (78)	45 (70)	
Positive/doubtful	24 (21)	19 (30)	
Missing	1 (1)	0 (0)	
Preoperative continence status			0,500**
Continent	76 (66)	40 (63)	
Incontinent	33 (28)	22 (34)	
Missing	7 (6)	2 (3)	
Body Mass Index (kg/m²)			
≤25.0	33 (29)	21 (33)	0.501**
25.1-30.0	63 (54)	36 (56)	
>30.0	20 (17)	7 (11)	
Mean (SD) preoperative IPSS score	6.80 (5.46)	8.14 (6.03)	0.087***
Mean (SD) preoperative KHQ score			
General health perceptions	78.66 (17.83)	77.34 (16.50)	0.468***
Incontinence Impact	86.49 (21.52)	80.21 (25.69)	0.072***
Role limitations	94.11 (14.62)	94.27 (14.91)	0.949***
Physical limitations	94.40 (14.40)	96.87 (8.33)	0.431***
Social limitations	97.89 (7.01)	98.61 (5.42)	0.562***
Personal relationships	95.31 (16.41)	92.90 (19.32)	0.536***
Emotions	90.72 (19.69)	86.98 (22.79)	0.130***
Sleep/Energy	80.03 (20.76)	78.64 (19.35)	0.442***
Severity measures	92.38 (15.72)	92.71 (15.10)	0.653***

*Independent t-test; **Fisher's exact/ X^2-statistics;***Mann-Whitney U test SD=Standard Deviation; statistical significance was defined as p<0,05

Table 2 : Cox regression for the time to urinary continence according to type of surgery

		Univariate analysis				Multivariate analysis			
	df	p-value	HR	CI (95%)		p-value	HR	CI (95%)	
				Lower	Upper			Lower	Upper
RARP vs. ORP	1	,008	1,548	1,123	2,132	,036	1,522	1,027	2,255
Age (≥65y vs. <65y)	1	,002	,588	,420	,825	,029	,6660	,454	,958
Risk Group	2	,300				,755			
- Intermediate vs. low	1	,380	,810	,506	1,297	,966	,989	,602	1,627
- High vs. low	1	,134	,686	,420	1,122	,615	1,159	,653	2,056
Nerve sparing status	2	,055				,572			
- Unilat. vs. nonnerve sparing	1	,372	1,289	,738	2,251	,732	1,110	,610	2,021
- Bilat. vs. nonnerve sparing		,034	1,719	1,041	2,837	,343	1,364	,718	2,589
Preoperative urine loss (incontinent vs. continent)	1	,012	1,554	1,103	2,191	,004	1,694	1,179	2,433
BMI	2	,705				,574			
- 25.1-30.0 vs. ≤ 25.0	1	,956	1,010	,712	1,431	,796	,953	,663	1,371
- >30.0 vs. ≤ 25.0	1	,475	,837	,513	1,365	,304	,763	,456	1,278

df= degrees of freedom; HR= hazard ratio; CI= confidence interval

Table 3 : Cox regression for the time to urinary continence according to type of surgery (sub analyses)

ORP vs. RARP	N	p-value	HR	CI (95%)	
				Lower	Upper
No correction for confounders	173	0.007	1.548	1.124	2.133
Correction for all confounders (age, D'Amico risk group, nerve sparing status, preoperative urine loss)	165	0.036	1.522	1.027	2.255
Subgroup bilateral nerve sparing	110	0.191	1.292	0.880	1.899
Subgroup intermediate risk group	89	0.287	1.264	0.821	1.944
Subgroup bilateral nerve sparing and intermediate risk group	71	0.516	1.173	0.724	1.900

HR= hazard ratio; CI= confidence interval

Table 4: Cumulative incidence of continence and average urine loss of patients at 1, 3, 6 and 12 months after ORP and RARP (24hpad test).

Time since catheter removal	Number (%) of continent patients			Average urine loss (gram)		
	ORP (n=109)	RARP (n=61)	p-value*	ORP (n=109)	RARP (n=61)	p-value**
1 month	46 (42%)	42 (69%)	**0.010**	108	50	**0.036**
3 months	85 (78%)	53 (87%)	0.162	16	14	0.816
6 months	102 (94%)	58 (95%)	0.540	10	4	0.492
12 months	105 (96%)	59 (97%)	0.896	2	4	0.454

*χ^2-test; ** Independent t-test; statistical significance was defined as p<0,05

Table 5: Comparison of the point prevalence of continence after radical prostatectomy at 1, 3, 6 and 12 months after surgery, according to type of surgery

	ORP	RARP	Odds Ratio (95% CI)	p value*
Secondary outcome parameters				
Point prevalence of continence, VAS-scale defined as ≤1/10				
At 1 month (115/62)	36 (31.3%)	37 (59.7%)	3.248 (1.708-6.175)	**0.000**
At 3 months (113/62)	70 (61.9%)	46 (74.2%)	1.766 (0.891-3.500)	0.132
At 6 months (113/62)	87 (77.0%)	51 (83.6%)	1.524 (0.680-3.416)	0.334
At 12 months (109/59)	84 (77.1%)	50 (84.7%)	1.653 (0.715-3.824)	0.315
Point prevalence of continence, 1h-pad test, defined as 0 gram				
At 1 month (110/61)	47 (42.7%)	36 (59.0%)	1.930 (1.023-3.642)	0.055
At 3 months (110/62)	75 (68.2%)	49 (79.0%)	1.759 (0.847-3.655)	0.157
At 6 months (109/62)	93 (85.3%)	56 (90.3%)	1.606 (0.594-4.344)	0.477
At 12 months (105/59)	88 (83.8%)	53 (89.8%)	1.706 (0.633-4.598)	0.353

*Fisher's exact test; statistical significance was defined as p<0,05