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Outcome of Robotic Radical Prostatectomy in Men Over 74

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Abstract

Introduction: We set out to evaluate outcomes in patients over 74 after robotic radical prostatectomy.
Materials and Methods: Six hundred forty-seven patients over 74 (≥75) were analyzed for preoperative factors (body mass index [BMI], American Society of Anestesiologists classification [ASA], prostate-specific antigen [PSA], International prostate symptome score [IPSS], International index of erectile function [IIEF]), operative and perioperative characteristics (technique, erythrocyte conc., complications), and histopathological results. After 12 months, following items were assessed: PSA, frequency of urine loss, number of pads used (including safety), incontinence at night, and potency as quantified by IIEF-5.
Results: Mean age in the group <75 was 64.8 years (range 46–74 years) and in the group ≥75 76.9 years (75–88). No statistically significant differences could be detected in terms of BMI, ASA score, or preoperative PSA, respectively. IPSS and IIEF were significantly worse in the group ≥75. Major complications (>Clavien-Dindo III) were found in 1.6% *vs*. 1.3% (≥75) of cases. Minor complications were encountered in 22.8% *vs*. 26.3% (≥75). There was a remarkably high percentage of locally advanced disease (73.3% *vs*. 71.0%) in both groups. Patients ≥75 showed a tendency toward more aggressive cancer and more frequent nodal involvement; we found a higher percentage of R1-resections (19.5% *vs*. 30.4%, $p < 0.05$) and PSA relapse after 1 year (12.3% *vs*. 22.8%, $p < 0.05$). Twelve months pad-free continence rate (69.9% *vs*. 63.2%) showed no statistically significant difference between both groups as did the preservation rate of erectile function.
Conclusion: We could show that robotic prostatectomy can be carried out safely with good functional and histopathological results in patients ≥75. It is therefore questionable if elderly patients can be precluded from curative radical treatment solely because of their age.

Keywords: prostate cancer, elderly, patients 75 years and older, robotic prostatectomy, outcome

Introduction

The maximum age for radical prostatectomy has always been a matter of debate. In keeping with American Urological Association (AUA) and European Association of Urology (EAU) guidelines, most urologists consider a live expectancy of greater than 10 years mandatory in patients undergoing radical prostatectomy.[1,2] Until recently, this was generally not the case in patients over 74 years and still those patients are very rarely being offered surgery.[3] In fact, only 10% of men over 74 with localized aggressive carcinoma and a Charleston comorbidity index of 0 receive radical treatment.[4] Consequently, these patients are more likely to receive ADT.

By contrast, the current life expectancy for men at this age in the United States[5] and Europe[6] stands at 10 years and is increasing at an average rate of 1 year per decade. For the 25% healthiest men of 75, life expectancy amounts to even 15 years.[4] Moreover, the proportion of men over 74 is estimated to reach 20% of the North American and European population by 2030.[7] It is expected that, in the near future, there will be a growing number of patients >75 with a life expectancy of 10 years and more and a diagnosis of prostate cancer.

Several studies could demonstrate that elder patients undergoing radical prostatectomy have more aggressive cancer that could have an impact on further life expectancy.[8–10] Therefore, radical surgical treatment is likely to result in significantly longer cancer-specific survival in this subgroup. Some

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Table 1. Preoperative Patient Demographics and Operative and Histopathological Outcomes

	<75	≥75	Sign.
Age	64.75 ± 6.54 [46–74]	76.92 ± 2.23 [75–88]	
OP-type			
Open	2.4%	14.1%	
Laparoscopic	7.4%	0%	
DaVinci-assisted	90.2%	85.9%	
BMI	27.60 ± 4.12	25.86 ± 3.51	$p < 0.01$
ASA			
ASA 1	9.6%	3.1%	
ASA 2	69.4%	66.2%	
ASA 3	21.0%	26.3%	
PSA	10.36 ± 9.93	11.27 ± 7.51	
TUR-P			
Yes	7.3%	12.1%	
No	92.7%	87.9%	
IPSS	8.70 ± 7.42	13.28 ± 9.24	$p < 0.01$
IIEF-15	35.90 ± 23.56	21 ± 18.84	$p < 0.01$
Bilateral nerve sparing	44.10%	43.40%	
pT			
1a	0.2%	0.0%	
1b	0.4%	0.0%	
1c	1.6%	0.0%	
2a	2.4%	4.3%	
2b	3.7%	1.4%	
2c	18.3%	23.2%	
3a	44.1%	46.4%	
3b	9.3%	15.9%	
4	19.9%	8.7%	
Gleason			
<7	22.7%	13.8%	
7a	22.0%	22.4%	
7b	27.8%	31.0%	
>7	27.5%	32.8%	
Margins			
R1	19.5%	30.4%	$p < 0.5$
R0	80.5%	69.6%	
pN			
N1	7.1%	11.8%	
N0	92.9%	88.2%	
Complications (C-D)			
III	1.6%	1.3%	
≤II	22.8%	26.3%	
No	75.7%	72.4%	

ASA = American Society of Anestesiologists classification; BMI = body mass index; IIES = International index of erectile function; IPSS = International prostate symptome score; OP = operation; PSA = prostate-specific antigen; TURP = transurethral resection of prostate.

studies could demonstrate prolonged overall survival[11] and favorable oncologic outcomes.[12,13]

In this context, robotic prostatectomy might be considered as treatment for elderly men because of minimal blood loss, faster recovery, and shorter hospital stay. It is widely agreed that robotic prostatectomy is a safe approach with a low percentage of significant complications, even in complex cases and elderly, comorbid patients.

If robotic prostatectomy significantly reduces cancer-specific and overall survival in patients over 74, functional parameters—that is, continence and potency—gain increasing interest. Yet, only a few groups have looked into functional outcomes following robotic prostatectomy in elderly patients, and only 3 of them focused on the age group of 75 years and older, with remarkably low patient numbers of 8 to 45.[14–17] To our knowledge, our study assesses the largest number of patients over 74 having had robotic prostatectomy.

Materials and Methods

Patients undergoing robotic prostatectomy are routinely enrolled in a prospective database. For this analysis, we reviewed our database for patients undergoing prostatectomy from October 2009 to November 2015. In total, 647 patients could be identified. We split this cohort into two age groups (<75 years, $n = 573$, mean age 64.75 ± 6.54 years; ≥75 years, $n = 74$, mean age 76.92 ± 2.23 years). Both groups were analyzed for preoperative (body mass index [BMI], American Society of Anestesiologists classification [ASA] risk stratification, transurethral resection of prostate [TURP], prostate-specific antigen [PSA], International prostate symptome score [IPSS], International index of erectile function-5 [IIEF-5]), operative, and perioperative characteristics (technique, erythrocyte conc., minor and major complications [Clavien Grade I-IIIa/IIIb-IV]), and the histological analysis of the prostate specimen. Patients who did not give their consent for follow-up were excluded from the analysis. Of note, mean initial PSA in the comparison group was above 10 ng/mL (10.4 ± 9.9), the percentage of locally advanced disease (pT3a, pT3b, and pT4) over 70% (71.0%), and the proportion of Gleason score of 7b and higher over 50% (55.3%). Thus, this group represents very well an up-to-date prostatectomy cohort, the majority of low-risk carcinomas currently being allocated to active surveillance.

After discharge, every patient received a questionnaire as a regular follow-up after 3, 6, and 12 months including the following items: PSA, frequency of urine loss, number of pads used (including safety pads), incontinence at night, and change of erectile function. Furthermore, we included the IIEF-5-questionaire.

Definition of biochemical recurrence was a PSA value of 0.2 ng/mL or above. Patients losing urine more than once a week or using more than a safety pad were considered incontinent.

Statistical analysis was performed using SPSS 23, for differences in the two groups we used *t*-tests and Pearson's chi-square tests in contingency tables. A significance level of 0.05 was chosen, results for 2 × 2 contingency tables in the follow-up are displayed as odds ratios.

Results

Preoperative and postoperative cohort parameters of the two groups are summarized in Table 1. Mean age in the group <75 was 64.8 years (range 46–74 years) and in the group ≥75 was 76.9 years (range 75–88). No statistically significant differences could be detected for BMI (27.6 ± 4.1 *vs.* 25.9 ± 3.5), ASA score (ASA3 21.0% *vs.* 26.3%), or preoperative PSA (10.4 ± 9.9 *vs.* 11.3 ± 7.5), respectively. Of note, both IPSS and IIEF were significantly worse in the group ≥75 (IPSS: 8.7 ± 7.4 *vs.* 13.3 ± 9.2; IIEF: 35.9 ± 23.6 *vs.* 21 ± 18.8, $p < 0.01$).

Table 2. Twelve Months: Follow-Up Outcomes

12 month follow-up	*<75*	*≥75*	*Odds ratio/ 95% confidence interval*	*Sign.*
PSA recurrence				
0.2	12.3%	22.8%	0.48	$p < 0.05$
<0.2	87.7%	77.2%	0.24–0.98	
Incontinence				
More 1/week	38.4%	41.0%	0.9	
Max. 1 time per week	61.6%	59.0%	0.51–1.57	
Incontinence				
At least 1 pad	30.1%	36.8%	0.74	
No pad/safety pad	69.9%	63.2%	0.44–1.23	
Change of erectile function				
Worse	79.9%	80.0%	0.98	
Unchanged	20.1%	20.0%	0.49–2.02	

A bilateral nerve sparing procedure was conducted for 44.1% of younger and for 43.4% of older patients.

Major complications (>Clavien-Dindo III) were noted in 1.6% *vs.* 1.3% (young *vs*. old) of cases. Minor complications occurred in 22.8% *vs.* 26.3% of the patients (Table 1).

On histopathological examination, our cohort stands out from other studies by a very high percentage of locally advanced disease in both groups (pT3a, pT3b, and pT4: 73.3% and 71.0%). Patients 75 years old and older showed a tendency toward more frequent lymph node involvement (7.1% *vs.* 11.8%) and more aggressive cancer (<Gleason 7: 22.7% *vs.* 13.8%; >Gleason 7: 27.5% *vs.* 32.8%); however, this trend did not reach statistical significance. There was a higher percentage of positive margins in the older cohort (19.5% *vs.* 30.4%, $p < 0.05$).

Biochemical and functional parameters on 12 months follow-up are summarized in Table 2 and Figure 1. We noted a significantly higher biochemical relapse (PSA >0.2 ng/mL) 12 months after surgery in patients 75 years old and older (young: 12.3%; old: 22.8%). While patients younger than 75 reached pad-free continence in 69.9%, this was the case for 63.2% of older men, the difference being statistically insignificant. Interestingly, we found a significantly higher rate of night time incontinence among young patients (19.7% *vs.* 8.1%, $p < 0.01$). Given a rate of bilateral nerve sparing of 44% (younger) and 43% (older), unchanged erectile function was obtained in 20.1% and 20.0%, respectively.

Discussion

Despite the numerous reports on oncological and overall results of radical prostatectomy in patients over 69, there are only a few studies focusing on the functional outcomes of robotic prostatectomy in men over 75.

In their retrospective study, Labanaris and Porres[16,17] assessed 2000 cases of robotic radical prostatectomies between 2006 and 2010. Among these patients, they identified 45 men over 74. Patients were divided according to age (<75 and ≥75 years). Continence rates did not significantly differ between both groups after 12 months (92.8% *vs.* 86.9%, $p = 0.05$). Regarding potency, they found significant differences (66.2% *vs.* 39.6%, $p < 0.001$), however, the analysis comprised only patients with bilateral nerve sparing.

Xylinas and colleagues[18] evaluated 22 patients over 74 after laparoscopic radical prostatectomy. On 1-year follow-up, continence rate was 82% and potency rate 36%, respectively. The authors considered laparoscopic prostatectomy safe for localized prostate carcinoma in elderly patients as oncological and functional results were shown to be good—however, there was still a higher rate of postoperative incontinence than in younger patients.

Shikanov and coworkers[15] found worse results for both continence and potency rates on 12-months follow-up in 1436 men after robotic prostatectomy. Continence rates were 66%, 63%, and 59%, and potency rates were 66%, 56%, and 46% at 65, 70, and 75 years of age, respectively. The age group of over 69 comprised 77, the age group of over 74 only 8 patients. Therefore, continence and potency rates are prone to bias because of small numbers.

Among 8295 patients after radical prostatectomy between 2009 and 2013, Mandel et al.[14] identified 166 men over 74 of whom only 27 had had robotic prostatectomy. Patients ≥75 years had their continence preserved in 86.5% (max. 1 safety pad per day) compared to 91.0% in the entire cohort. Potency rates were 31.3% *vs*. 54.6% (IIES-5 score of 18 or higher) on 12-month follow-up. The authors concluded that recovery of continence and potency is clearly age dependent. Nevertheless, functional results in elderly men and particularly in those over 74 were still good. Using the same database, the group could show that these patients harbored a higher rate of aggressive and locally advanced tumors, resulting in a higher percentage of positive surgical margins.[10]

Greco et al.[19] assessed 203 men after robotic prostatectomy of whom 23 (11%) were aged ≥70 years. Surgical complications were evenly distributed among both groups, however, older men could be shown to have lower continence on 6-months follow-up (60% *vs.* 79%, $p = 0.04$). However,

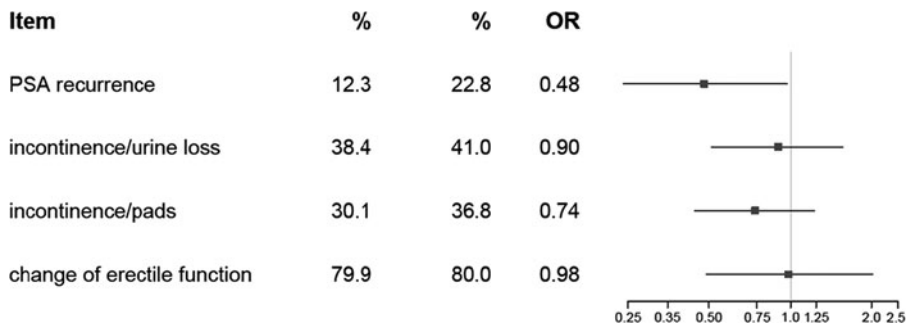

FIG. 1. Percentages and OR for the rates of biochemical relapse, incontinence and preserved erectile function after 12 months in patients <75 and patients ≥75. O = odds ratio; PSA = prostate-specific antigen.

after 12 months, they reached the continence level of the younger group (83% *vs.* 89.2%, $p = 0.54$).

To our knowledge, this report of 74 patients over 74 is the largest analysis of oncologic and functional parameters in patients ≥75 years who underwent robotic prostatectomy. On histopathological examination, patients 75 years and older showed a tendency toward more aggressive cancer, however, this trend did not reach statistical significance in our cohort. In accordance with previous reports, there was a higher proportion of positive margins in the older cohort (19.5% *vs.* 30.4%, $p < 0.05$). Most notably, neither complication (1.6% *vs.* 1.3%) nor 12 months continence (69.9% *vs.* 63.2%) rate showed a statistically significant difference between both groups. Full preservation of potency was achieved in only 20% in both groups, which is clearly worse than in other reports. However, our cohort stands out by the high percentage of locally advanced disease in both groups (pT3a, pT3b, and pT4: 73.3% and 71.0%), allowing for bilateral nerve sparing in only 44% and 43%, respectively. There was also a significantly higher chance for biochemical relapse for patients 75 years and older.

The oncological outcome in our cohort is in line with previous reports. Mandel and associates[10] found significantly higher rates for both positive surgical margins (23.2%) and biochemical recurrence (28.2%) in their patients 75 years and older. Our 12 months pad-free continence rate of 63.2% is better than some reports[15] and worse than others,[14,17] but, in our view, acceptable for a population ≥75 after radical prostatectomy—given a general prevalence of incontinence in this age group of 15% to 25%.[19]

The potential benefit from prostatectomy in the population ≥75 depends on the aggressiveness of the prostate cancer on one hand and the complication and morbidity rate of the procedure on the other. It has been shown by our and other groups that elderly men harbor significantly more aggressive cancer and that robotic prostatectomy can be carried out safely with good functional results. Given the fact that cT2 prostate cancer causes in up to 27% cancer-specific death within 15 years for men over 74,[20] radical surgical treatment is likely to result in significantly longer cancer-specific survival in this subgroup, together with good quality of life. It is therefore questionable whether elderly patients can be precluded from curative radical treatment solely because of their age. Moreover, many of the elderly suffer from obstructive symptoms of benign prostatic enlargement and are likely to receive medical or surgical treatment. The beneficial effect on outflow obstruction might be considered when planning robotic prostatectomy for a patient 75 years old or older.

There are several limitations to our study. (1) This is a retrospective cohort analysis and therefore of restricted evidence level. (2) The second one is that our results might not be representative for all men over ≥74, as they are generated from a highly selected and otherwise healthy group of patients. (3) Thirdly, our follow-up is definitely too short to reveal an impact on biochemical, cancer-specific, and overall survival. (4) Finally, some patients might experience further functional restoration of continence and potency over time.

Despite these limitations, this study adds important knowledge to the literature, showing that in patients over 74 with prostate carcinoma robotic prostatectomy might be preferable to conservative treatment.

Conclusion

We could show that robotic prostatectomy can be carried out safely with good functional and histopathological results in patients ≥75. Given the fact that elderly men harbor more aggressive cancer, we conclude that elderly patients might well benefit from robotic prostatectomy compared to conservative treatment.

Ethical Statement

All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (Ethikkommission der Universität Witten-Herdecke).

Author Disclosure Statement

No competing financial interests exist.

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Abbreviations Used

BMI = body mass index
ASA = American Society of Anestesiologists classification
IIEF = International index of erectile function
IPSS = International prostate symptome score
PSA = prostate-specific antigen
OR = odds ratio
TUR-P = transurethral resection of prostate