Robotic-assisted Radical Prostatectomy in Men ≥75 Years of Age. Surgical, Oncological and Functional Outcomes

APOSTOLOS P. LABANARIS, JORN H. WITT and VAHUDIN ZUGOR

Department of Urology and Pediatric Urology, Prostate Center Northwest, St. Antonius Medical Center, Gronau, Germany

Abstract. *Background: The aim of this study is to evaluate the surgical, the oncological and the functional outcomes in men ≥75 years of age undergoing robot-assisted radical prostatectomy (RARP). Patients and Methods: The records of N=2000 men who underwent RARP from February 2006 to April 2010 were retrospectively reviewed. A total of 45 patients who were ≥75 years of age were indentified. A comparison was performed between the overall patient cohort and the aforementioned patients. The analyzed parameters included: minor and major postoperative complications, postoperative Gleason score, pathological stage, positive-margin status, continence and potency in 12 months, disease-specific mortality and presence of biochemical progression at the follow-up period. Results: The following results reflect the comparison of the overall cohort of patients vs. the cohort of patients who were ≥75 years of age. A statistical difference of the analyzed parameters was observed only minor complications 11.4% vs. 15.5% (p<0.05), neurovascular bundle (NVB) preservation 65.7% vs. 51.1% (p<0.05) and potency after 12 months 66.2% vs. 39.6% (p<0.001). Major complications were noted in 1.3% vs. 2.2% of cases. A Gleason score <7 was noted in 42.8% vs. 37.3%, a Gleason score 7 in 47.7% vs. 51.1% and a Gleason score >7 in 9.5% vs. 11.6%. Organ-confined disease was noted in 73.5% vs. 68.8%, extraprostatic extension in 25.2% vs. 31.2% and positive surgical margin status was encountered in 8.9% vs. 11.1% of cases. At 12 months, 92.8% vs. 86.9% of patients were continent and 66.2% vs. 39.6% were potent. After a median follow-up of 17.2 months no disease-specific mortality was evident and 95.5% were free of biochemical progression in the cohort of patients who were ≥75 years of age. Conclusion: Our findings suggest that RARP in patients ≥75 years of age is a safe surgical procedure with limited complications, excellent oncologic and continence outcomes as well as acceptable potency outcomes. Nevertheless, RARP should be limited to a selected cohort of patients with a good overal health status and an individual life expectancy of more than 10 years in order for the oncological advantages of surgery to be achieved.*

Treatment decision-making in localized prostate cancer (PCa) in aged patients is complex. Published data suggest that otherwise healthy older men with localized PCa may not be receiving potentially life prolonging treatment, as a result of the perception that they are unlikely to benefit from these therapies (1). Men younger than 60 years of age who have clinically localized disease are 25 times more likely to undergo radical prostatectomy than men aged 70 years or older (2). In contrast, decreased rates of potentially curative therapy do not seem to be influenced by tumor grade or comorbidity, indicating that a patient's chronological age alone may be the factor inappropriately influencing treatment decisions (3). The upper age limit for radical prostatectomy as a curative treatment for localized PCa is controversial. Historically, radical prostatectomy was rarely offered to patients older than 70 years due to concern for short life expectancy and poor functional outcomes. This paradigm is currently being challenged in the face of an expanding elderly population, since data indicate that the average survival of a 70-year-old man after such surgery is 13 years (4). With the ageing of the population and given the fact that >70% of PCa is diagnosed in men aged >65 years, it seems certain that an increasing number of patients over 70 years old with significant life expectancy will present with PCa to urologists (5). Although there are no randomized clinical trials that have demonstrated a survival advantage of radical prostatectomy over watchful waiting in this cohort of patients, several studies have recently demonstrated adequate

Correspondence to: Apostolos P. Labanaris, MD, Ph.D., Prostate Center Northwest, Department of Urology and Pediatric Urology, St. Antonius Medical Center, Moellenweg 22, 48599 Gronau, Germany. Tel: +49 25629157114, Fax: +49 25629152105, e-mail: labanaris@web.de

Key Words: Robot-assisted laparoscopic radical prostatectomy, elderly patients, prostate cancer, surgical outcomes, oncological outcomes, functional outcomes, prostate specific antigen.

oncological outcomes, as well as a statistically significant and clinically important improvement in disease-specific mortality in patients undergoing radical prostatectomy (6-9).

During recent years robotic-assisted laparoscopic radical prostatectomy (RARP) has become profoundly popular among urologists for the treatment of localized PCa. Although there might be a lack of randomised trials, there is reasonable evidence to suggest that RARP is a well-tolerated, safe, and efficacious intervention for the management of localised PCa (10, 11). Furthermore, RARP is an appealing treatment option for clinically localized PCa due to fast recovery, less blood loss, improved cosmesis and surgical outcomes comparable to those for open radical prostatectomy. The objective of this study was to evaluate the surgical, oncological and functional outcomes in men ≥75 years of age undergoing RARP.

Patients and Methods

The records of 2000 men who underwent RARP from February 2006 to April 2010 were retrospectively reviewed. All perioperative and postoperative data were recorded prospectively in our database. A total of 45 (2.25%) of patients who were ≥75 years of age were identified. A comparison was performed between the overall patient cohort and the aforementioned patients.

RARP was performed using the Da Vinci Robotic 4-Arm System (Intuitive Surgical, Sunnyvale, CA, USA) *via* a transperitoneal approach. Pelvic lymph node dissection was performed in patients with a prostate specific antigen (PSA) level >10 ng/ml and/or Gleason score >6. Bilateral neurovascular bundle (NVB) preservation was attempted in patients with a PSA level <10 ng/ml and/or Gleason score ≤7. Men with preoperative impotence did not undergo NVB preservation. Patients who underwent a unilateral or a non nerve-sparing surgery were excluded from sexual function analysis. The procedures in both patient cohorts were performed by five experienced RARP surgeons by a standard transperitoneal approach as reported previously by our group (12).

The compared parameters between the two groups included patient preoperative clinicopathological characteristics [age, body mass index (BMI), prostate size and PSA values], intraopeoperative characteristics [NVB preservation, estimated blood loss, and skin-to-skin operative time], postoperative oncological characteristics [tumor volume, Gleason score, pathological stage and positive surgical margins (PSM)], minor complications [retention, urinary leakage, urinary tract infection, lymphocele, superficial abscess and subcutaneous emphysema] and major complications [infected lymphocele, bowel injury, acute renal failure and re-operation], duration of catheterization, continence, potency, biochemical progression and disease-specific mortality during the follow-up period. Postoperative complications and re-interventions encountered up to 30 days postoperatively were stratified by the Clavien classification (13) and were characterized as minor (Clavien's grade I-IIIa) and major (Clavien's grade IIIb-IVa) postoperative complications. Hemorrhage was defined as greater than 500 ml blood loss during the operation. A PSM was defined as tumor at the inked surface of the specimen. Biochemical progression was defined as PSA ≥0.2 μg/l after nadir or never reaching nadir. In all patients, after surgery, only PSA surveillance was performed with external radiation therapy and/or hormonal therapy at the onset of a rise in PSA. In cases were adjuvant therapy was initiated, patients were further excluded from the follow-up of biochemical progression but not from the follow-up for disease-specific mortality.

All patients underwent cystography postoperatively at day 4. The catheter was then removed if no extravasation was recorded. If extravasation was present, the catheter was left in place for seven additional days. Functional results regarding urinary continence were evaluated prospectively only 12 months after surgery. Urinary continence was defined as no pad use and/or no urinary leakage. Functional results regarding potency were evaluated prospectively only 12 months after surgery. Potency was defined as erections sufficient for penetration with or without phosphodiesterase inhibitors. The analysis of potency was limited to patients who were potent before RARP, had bilateral nerve-sparing surgery, and had a follow-up of ≥12 months with no adjuvant therapy. Once a patient was potent or continent, he was to be considered potent or continent on further analysis. The median postoperative follow-up of the patients was 17.2 months (range 3-36 months). For the comparison between two groups of continuous values the Student *t*-test was used. For comparison between 3 or more groups the one-way ANOVA with the Tukey correction for multiple comparisons was used. For the comparison of binomial values, the Chi-square test was used. Simple linear regression was used in order to test the effect of one continuous parameter against another. A *p*-value of <0.05 was considered significant.

Results

The preoperative, intraoperative and postoperative clinico-pathological characteristics of the two groups are listed in Table I. The following results reflect the comparison of the overall cohort of patients *vs*. the cohort of patients who were ≥75 years of age. A statistical difference of the analyzed parameters was observed only in the age of 63 *vs*. 76 years old ($p<0.001$), minor complications 11.4% *vs*. 15.5%. ($p<0.05$), NVB preservation 65.7% *vs*. 51.1% ($p<0.05$) and potency after 12 months 66.2% *vs*. 39.6% ($p<0.001$).

The median PSA value was 10.3 ng/ml *vs*. 9.3 ng/ml. Major complications were noted in 1.3% *vs*. 2.2% of cases; one patient (2.2%) from the elderly patient cohort exhibited a major complication which was a bowel injury, that was indentified and corrected intraoperatively without any further complications. Minor complications were encountered in 11.4% *vs*. 15.5% of the patients; seven patients (15.5%) from the elderly patient cohort exhibited minor complications which were urinary leakage in four patients, which was treated by leaving the catheter in place for an additional seven days, and urinary retention in three cases, which was treated by inserting a new catheter and by removing it two days later.

Organ-confined disease was noted in 73.5% *vs*. 68.8%, extraprostatic extension in 25.2% *vs*. 31.2% and PSM status was encountered in 8.9% *vs*. 11.1% of cases. Pelvic lymph node dissection was performed in 1623 patients (81.2%) of the overall cohort out of whom 64 cases (3.2%) were positive. In the elderly patient cohort, pelvic lymph node dissection was performed in 39 patients (86.7%) out of

Table I. *Preoperative, intraoperative and postoperative clinicopathological characteristics of the two groups analysed.*

Parameters	Overall patient cohort	Patients ≥75 years of age	*p*-values
Patients	2000	45	
Age in years	63 (38-79)	76 (75-79)	<0.05
Body Mass Index (BMI)	26.7 kg/m^2 (19-51 kg/m^2)	26.9 kg/m^2 (22-36 kg/m^2)	
Prostate size	56.1 g (10-170 g)	52.8 g (30-102 g)	<0.05
Prostate specific antigen	10.3 ng/ml (0.3-220 ng/ml)	9.3 ng/ml (3.8-29.6 ng/ml).	
Neurovascular bundle preservation	65.7%	51.1%	<0.05
Blood loss	160 ml (60-1500 ml)	131 ml (50-300 ml)	
Minor complications	11.4%	15.5%	
Major complications	1.3%	2.2%	
Operative time	156 min (80-465 min)	143 min (100-240 min)	
Length of catheterisation	5.5 days (5-31 days)	6.1 days (5-30 days)	
Gleason score			
<7	42.8%	37.3%	<0.05
=7	47.7%	51.1%	<0.05
>7	9.5%	11.6%	<0.05
Stage			
Confined disease	73.5%	68.8%	<0.05
Extraprostatic extension	25.5%	31.2%	<0.05
Positive margins	8.9%	11.1%	<0.05
Tumor in specimen (%)	16.1% (1-99%)	17.8% (2-99%)	
Positive lymph nodes	3.2%	4.4%	
Continence (12 months)	92.8%	86.9%	
Potency (12 months)	66.2%	39.6%	<0.001

whom 2 cases (4.4%) were disease-positive. There was no significant difference in positive lymph nodes when comparing both cohorts of patients. From the eldery patient cohort, all 45 patients were preoperatively continent and the one-year functional outcomes assessment involved 30 patients (66%), out of whom 26 (86.9%) were continent, with the remaining four exhibiting only mild incontinence (defined as the requirement for 1-2 pads daily).

Eleven patients (24.4%) had been impotent preoperatively and 11 patients (24.4%), due to tumor status, did not undergo a (NVB) sparing procedure. Thus, 23 (51.1%) underwent a bilateral NVB sparing procedure, of whom the assessment of one-year functional outcomes involved 16 patients (35.5%). When comparing both patient cohorts at 12 months, 92.8% *vs*. 86.9% of patients were continent and 66.2% *vs*. 39.6% were potent.

After a median follow-up of 17.2 months (range 3–36 months), no disease-specific mortality was evident and 43 patients (95.5%) were free of biochemical progression in the cohort of patients who were ≥75 years of age.

Discussion

Selecting appropriate candidates for surgical treatment of PCa is critically important in the elderly population. Although a life-expectancy of ≥10 years has emerged as an accepted prerequisite for considering potentially curative therapy, the average survival of a 70-year-old man is 13 years, whereas the one of a 75-year old man is 10 years (4). Despite this fact, many urologists avoid definitive treatment for localized PCa in older patients based on age alone, regardless of life-expectancy.

Albertsen *et al*. (14) reported on 767 men with localized PCa treated expectantly or with hormonal therapy, and found that PCa can cause significant mortality even in men aged ≤70 years. Although men aged 70 to 74 with a biopsy Gleason sum of 2-3 were found to have a minimal risk of PCa-related death, 32%, 40% and 60% of men with biopsy Gleason sums of 6, 7, and 8-10, respectively, died from PCa. For patients with low-grade disease, the tumor is slow-growing, treatment complications are important, and the risk of dying from competing causes exceeds the risk of cancer death. Moreover, benefits from potentially curative therapy are restricted to men with no comorbidity and are conditional on patients' preferences. In particular, an individual patient's level of discomfort associated with leaving his disease untreated, significantly influences the preferred treatment. For patients with high-grade disease, potential curative therapy should be seriously considered in, otherwise, reasonably healthy men (15).

Studies show that surgical treatment of PCa in the elderly offers comparable outcomes to those in younger men, with significant gains in life expectancy and in quality of life. In a series of 326 men who were aged ≥70 years and who had

undergone radical prostatectomy, multivariate models for predicting PCa recurrence did not show that age was a predictor of recurrence (16). Furthermore, Alibhai *et al*. (17) reported the effect of radical prostatectomy on life expectancy and quality-adjusted life expectancy in elderly men. They found that for men with biopsy Gleason sums of 5-7, radical prostatectomy resulted in significant gains in life expectancy and quality-adjusted life expectancy up to 75 years of age, whereas in patients with Gleason 8-10 disease, these gains were apparent in patients up to 80 years of age. It has been well established that older men are diagnosed with more aggressive tumors (18) which may lead to a significant cancer-specific mortality (14), while several reports have shown that the oncological outcomes of radical prostatectomy in elderly and younger men are equivalent (7-9). As seen throughout our data, although older men had more aggressive tumors, no significant difference was evident when comparing them to the overall patient cohort.

Current studies inadequately address individual patient characteristics when deciding whether to treat older men for PCa. There is a need for an individualized approach by estimating the remaining life expectancy. The estimation of the remaining life expectancy could be performed with the use of comorbidity assessment. Various tools measuring comorbidity in elderly people with cancer have been validated in contemporary literature. The Charlson Comorbidity Index (CCI) and the Adult Comorbidity Index-27 (ACE-27) are two such tools which have been proven reasonably accurate for assessing 10-year survivals in men with localized PCa (19). This can allow clinicians to individualize treatment decisions for men who are the best candidates to live long enough to reap the benefits of surgery. Age alone should not be used when deciding whether aggressive treatment is appropriate; rather, the overall health should be assessed by using a validated metric for comorbidity.

Pfitzenmaier *et al*. (20) evaluated and compared the survival in PCa patients who underwent radical prostatectomy before or after the age of 70 years. The 10-year PSA-free survival for old and young patients respectively was 51.8 and 57.4% (p=0.721), the 10-year disease-specific survival was 92.3 and 97.6% (p=0.342), the 10-year metastasis-free survival was 86.9 and 89.7% (p=0.713), and the 10-year overall-survival was 78.1 and 71.2% (p=0.565). They concluded that in a well-selected healthy, elderly population, the survival outcome is not worse than that of younger patients and that curative treatment should be recommended.

Pierorazio *et al*. (21) examined the survival outcomes of 386 patients aged ≥70 years who underwent radical prostatectomy. The median follow-up was 6.5 years. The PCa-specific survival rate was 97.6%, 94.0% and 90.2% at 5, 10 and 15 years after radical prostatectomy, respectively. The respective cardiovascular survival rate was 99.5%, 97.6% and 92.5%, and the overall survival rate was 93.1%, 82.5% and 68.9%, respectively. They concluded that, if appropriately selected, older men have excellent overall and PCa-specific survivals after radical prostatectomy and that the benefits of surgery should be weighed against the increased risks of surgical and anaesthetic complications.

Xylinas *et al*. (22) reported on 22 patients older than 75 years who underwent laparoscopic radical prostatectomy. With a median follow-up of 42 months, no patient had died and only five had a biochemical recurrence. At 12-month follow-up, 82% of patients were continent and 36% potent. They concluded that laparoscopic RP is feasible for localized PCa in elderly well-selected patients with satisfactory oncological and functional outcomes although the incontinence rate is increased compared to younger patients. As seen throughout our data, after a median follow-up of 17.2 months no mortality was evident and 95.5% were free of biochemical progression in the eldery patient cohort.

During the past years RARP has become profoundly popular among urologists for the treatment of localized PCa. Although there might be a lack of randomised trials, there is reasonable evidence to suggest that RARP is a well-tolerated, safe, and efficacious intervention for the management of localised PCa (10, 11). Furthermore, RARP is an appealing treatment option for clinically localized PCa due to fast recovery, less blood loss, improved cosmesis and surgical outcomes comparable to open radical prostatectomy.

Greco *et al*. (23) assessed the outcomes of elderly men compared to younger men with PCa treated with RARP. Out of the 203 men, 23 were aged ≥70 years. The pathological RARP Gleason grade was significantly greater in older men. They concluded that the outcomes of RARP in elderly men are largely comparable to those in younger men, with the exception of higher pathological Gleason grade and a transient delay in return of continence.

Although our study benefits from reporting on the largest cohort of patients ≥75 years of age undergoing RARP, ever to have been analyzed, there are three certain limitations that should be addressed. The first one is that in our study, older patients represent a highly selected, healthy and motivated population. As such, our results may not be applicable to the average man with localized PCa of corresponding chronological age. The second limitation is that we assessed only one-year functional outcomes out of the elderly patients. Out of the patients included in this analysis, only 66% (N=30) were included regarding continence rates, due to our inadequate follow-up period (3-36 months), of whom 53.3% underwent bilateral NVB sparing. Additionally, included patients could possibly exhibit further improvement in the future, especially regarding potency rates. The third limitation is the inadequate follow-up period regarding PSA-free survival and disease-specific survival.

Despite these limitations, our findings suggest that RARP in patients ≥ 75 years of age is a safe surgical procedure with

limited complications, excellent oncological and continence outcomes, as well as acceptable potency outcomes. Nevertheless, RARP in patients ≥ 75 years old should be limited to a selected cohort of patients with a good health status and an individual life expectancy of more than 10 years, in order to deliver the oncological advantages of surgery.

References

1 Menon M, Parulkar BG and Baker S: Should we treat localized prostate cancer? An opinion. Urology *46*: 607-616, 1995.

2 Yan Y, Carvalhal GF, Catalona WJ and Young JD: Primary treatment choices for men with clinically localized prostate carcinoma detected by screening. Cancer *88*: 1122-1130, 2000.

3 Bennett CL, Greenfield S, Aronow H, Ganz P, Vogelzang NJ and Elashoff RM: Patterns of care related to age of men with prostate cancer. Cancer *67*: 2633-2641, 1991.

4 Minino AM and Smith BL: Deaths: preliminary data for 2000. Natl Vital Stat Rep *49*: 1-40, 2001.

5 Crawford ED: Epidemiology of prostate cancer. Urology *62*: 3-12, 2003.

6 Holmberg L, Bill-Axelson A, Helgesen F, Salo JO, Folmerz P, Häggman M, Andersson SO, Spångberg A, Busch C, Nordling S, Palmgren J, Adami HO, Johansson JE and Norlén BJ: Scandinavian Prostatic Cancer Group Study Number 4: A randomized trial comparing radical prostatectomy with watchful waiting in early prostate cancer. N Engl J Med *347*: 781-789, 2002.

7 Magheli A, Rais-Bahrami S, Humphreys EB, Peck HJ, Trock BJ and Gonzalgo ML: Impact of patient age on biochemical recurrence rates following radical prostatectomy. J Urol *178*: 1933-1937, 2007.

8 Malaeb BS, Rashid HH, Lotan Y, Khoddami SM, Shariat SF, Sagalowsky AI, McConnell JD, Roehrborn CG and Koeneman KS: Prostate cancer disease-free survival after radical retropubic prostatectomy in patients older than 70 years compared to younger cohorts. Urol Onc Sem Orig Invest *25*: 291-297, 2007.

9 Siddiqui SA, Sengupta S, Slezak JM, Bergstralh EJ, Leibovich BC, Myers RP, Zincke H and Blute ML: Impact of patient age at treatment on outcome following radical retropubic prostatectomy for prostate cancer. J Urol *175*: 952-957, 2006.

10 Ficarra V, Cavalleri S, Novara G, Aragona M and Artibani W: Evidence from robot-assisted laparoscopic radical prostatectomy: a systematic review. Eur Urol *51*: 45-56, 2007.

11 Ficarra V, Novara G, Artibani W, Cestari A, Galfano A, Graefen M, Guazzoni G, Guillonneau B, Menon M, Montorsi F, Patel V, Rassweiler J and Van Poppel H: Retropubic, laparoscopic, and robot-assisted radical prostatectomy: a systematic review and cumulative analysis of comparative studies. Eur Urol *55*: 1037-1063, 2009.

12 Witt JH, Zugor V, Wagner C, Shuette A and Labanaris AP: Robot-Assisted Radical Prostatectomy, Laparoscopy – An Interdisciplinary Approach, Ivo Meinhold-Heerlein (Ed.). ISBN: 978-953-307-299-9, InTech, Available from: http:// www.intechopen.com/articles/show/title/robot-assisted-radical-prostatectomy, 2011.

13 Dindo D, Demartines N and Clavien PA: Classification of surgical complications: A new proposal with evaluation in a cohort of 6336 patients and results of a survey. Ann Surg *240*: 205-213, 2004.

14 Albertsen PC, Hanley JA, Gleason DF and Barry MJ: Competing risk analysis of men aged 55-74 years at diagnosis managed conservatively for clinically localized prostate cancer. JAMA *280*: 975-980, 1998.

15 Mazur DJ and Hickam DH: Patient preferences for management of localized prostate cancer. West J Med *165*: 26-30, 1996.

16 Catalona WJ and Smith DS: Cancer recurrence and survival rates after anatomic radical retropubic prostatectomy for prostate cancer: intermediate-term results. J Urol *160*: 2428-2434, 1998.

17 Alibhai SM, Naglie G, Nam R, Trachtenberg J and Krahn MD: Do older men benefit from curative therapy of localized prostate cancer? J Clin Onc *21*: 3318-3327, 2003.

18 Jani AB, Johnstone PA, Liauw SL, Master VA and Brawley OW: Age and grade trends in prostate cancer (1974 –2003): a Surveillance, Epidemiology, and End Results Registry analysis. Am J Clin Oncol 31: 375-8, 2008.

19 Walz J, Gallina A, Saad F, Montorsi F, Perrotte P, Shariat SF, Jeldres C, Graefen M, Bénard F, McCormack M, Valiquette L and Karakiewicz PI: A nomogram predicting 10-year life expectancy in candidates for radical prostatectomy or radiotherapy for prostate cancer. J Clin Oncol *25*: 3576-3581, 2007.

20 Pfitzenmaier J, Pahernik S, Buse S, Haferkamp A, Djakovic N and Hohenfellner M: Survival in prostate cancer patients ≥70 years after radical prostatectomy and comparison to younger patients. World J Urol *27(5)*: 637-642, 2009.

21 Pierorazio PM, Humphreys E, Walsh PC, Partin AW and Han M. Radical prostatectomy in older men: survival outcomes in septuagenarians and octogenarians: BJU Int *106(6)*: 791-795, 2010.

22 Xylinas E, Ploussard G, Paul A, Gillion N, Vordos D, Hoznek A, De La Taille A, Abbou CC and Salomon L: Laparoscopic radical prostatectomy in the elderly (>75 years old): oncological and functional results. Prog Urol *20(2)*: 116-120, 2010.

23 Greco KA, Meeks JJ, Wu S and Nadler RB: Robot-assisted radical prostatectomy in men aged ≥70 years. BJU Int *104*: 1492-1495, 2009.

Received February 14, 2012
Revised April 11, 2012
Accepted April 17, 2012