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Radical prostatectomy in the treatment of clinically localized prostate cancer

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Abstract

***Objectives*:** Survival results for 367 radical prostatectomies performed on a caucasian portugueses population of patients in an academic hospital are presented and compared with results obtained in other world-renowned centers of activity.

***Patients and Methodology*:** We reviewed the reports of 367 patients treated between 1991 and 2000. All patients had previous histological cancer confirmation by transrectal tru-cut biopsy. The radical prostatectomy was based on the Walsh technique. The clinical evaluation and pathological extent of disease was based on the UICC-TNM (1992 version) classification, and histological grading according to the Gleason method. Patients were divided in groups according to total PSA basal level. Relapse was defined by the biochemical criteria of a PSA greater than 0.2 ng/ml in two successive determinations. Adjuvant radiotherapy was administered to patients with tumors classified as pT3b-c or pN positive and to those with pT3a only if they were deemed to have bad prognostic factors.

***Results*:** We found 57.2% patients with organ confined cancer, 38.2% with extraprostatic cancer (pT3), and 4.6 % with metastatic regional lymph node (pN positive). 15% of patients had a Gleason score G2-4, 68.3% G5-7 and 16.3% G8-10. We observed 7.6% of patients with a PSA range between 0-4 ng/ml, 37.9% between 4.1-10 ng/ml, 36.2% between 10.1-20 ng/ml and 18.3% with more than 20 ng/ml. The overall 5-year biochemical failure-free survival value for our 367 patients was 73.9% (Fig.1) and the values for the pT2, pT3, and pTN+ groups were 78.8 %, 75.2 %, 17.3 %, respectively (p= 0.00025) (Fig. 2). The result by Gleason score G2-4, G5-7, G8-10 was 87.1%, 73.0%, and 55.3%, respectively, (p=0.00016). The results by PSA groups 0-4 ng/ml, 4.1-10ng/ml, 10.1-20ng/ml and greater than 20 ng/ml were 100%, 78.5 %, 69.6% and 63.7% respectively, (p= 0.00029).

***Discussion and Conclusions*:** There was strong evidence that radical prostatectomy favorably alters the survival history of the patient. Prognostic factors allow us to select those with the greatest cure potential, but they are unsufficient to select a curable group with certainty. The results presented in referenced world-renowned hospitals, can be obtained in others hospitals, putting this surgical procedure as a routine one

Key Words: prostate cancer, radical prostatectomy, prognostic factors, survival, prostate specific antigen (PSA)

Introduction

The introduction of new and more efficient diagnostic techniques, namely, total prostate specific antigen (PSA), transrectal ultrasonography (TRUS) a more advanced biopsy method, in conjunction with a major increase in the public consciousness of prostate cancer has dramatically increased the diagnosed cases of prostate cancer in the last decade (1), particularly in those older than 65 years of age. Data from the National Cancer Institute (NCI) of the USA (2), showed that the incidence actually increased between 1978 and 1996 but appears to have decreased slowly after 1992. On the other hand, the mortality rate did not increase, but to the contrary has declined slowly after the years 1992-94. The reason for this decline has been difficult to explain. In Europe the incidence of prostate cancer has accompanied these data from the USA albeit with somewhat lower rates (3). Prostate cancer has been the second leading cause of cancer deaths after lung cancer (3) and as such is clearly a grave public health problem. In spite of the evolution of new therapeutic agents the percentage of cured patients is still unsatisfactory, and treatment controversial because the natural history of prostate cancer is relatively unknown (4) and the fact that many statistically designed studies in progress have not had sufficient time to draw definitive conclusions (5). It has been observed that a large proportion of those who have had radical prostatectomy have a life span similar to those in the general population. Their survival rate at 5, 10 and 15 years vary between 96-98%, 90-94%, and 82% respectively (6). The survival rates, free of disease based on biochemical criteria (PSA), for 5 and 10 years respectively vary between 69-83% and 47-78% (7). For this reason, radical prostatectomy is considered as the gold standard against which other treatments should be compared.

Our objective is to present results of radical prostatectomy obtained in a caucasian portuguese population and performed in an academic hospital center and compare these results with those obtained in world-renowned centers of reference.

Patients and Methodology

We treated 367 patients between 1991 and 2000. The patient's characteristics are shown in Table 1. We routinely obtained histological confirmation by a transrectal tru-cut biopsy. The criteria for selection was based on the presence of clinically localized prostatic carcinoma and a life expectancy of more than 10 years. We obtained the informed consent of all patients to voluntarily opt for surgery based on the unbiased information and factors associated with each individual. The clinical evaluation consisted of a digital rectal examination (DRE), PSA determination and routine exams. In the case of more extensive disease evaluation we utilized a TRUS, bone scan (not required when the PSA was less than 10 ng/ml) and MRI (not required when the tumor histology, in biopsy was inferior to G8-10). We utilized a radical prostatectomy technique based on the Walsh method (8). For a clinical evaluation and to determine the pathological extent of the disease we utilized the UICC-TNM classification, 1992 version (9). For histological grade evaluation, we used the combined Gleason method (10). We divided the patients in the four classical PSA groups: 0-4 ng/ml, 4.1-10 ng/ml, 10.1-20 ng/ml and greater than 20 ng/ml. The definition of relapse was based on the biochemical criteria determined by a PSA level greater than 0.2 ng/ml, in two successive determinations. We instituted radiation therapy in 97 patients which had tumors classified as pT3b-c or pN positive and in those with pT3a, if they were deemed to have bad prognostic factors. In the 48 first cases we also used neoadjuvant treatment with androgen deprivation (MAB). The data for these patients were stored using a specially designed database utilizing the Microsoft Access database program. The evaluation of survival was based on the actuarial method of Kaplan-Meier and statistical significance was evaluated using the Cox Proportional Hazards method. These survival curves and the statistical significance of the various groups presented were determined using the S-PLUS 2000 statistical package.

Pts. with clinically localized prostate cancer	**367**
Mean age (years)	**65.1 (range 45-76)**
Mean follow up (months)	**36 (range 1-110)**
No. Pathological stage (%)	
pT2	210 (57.2)
pT3	140 (38.2)
pT3a	59 (42.1)
pT3b	38 (27.2)
pT3c	43 (30.7)
No. Gleason score (%)	
G2-4	49 (15)
G5-7	218 (68.3)
G8-10	52 (16.3)
No. PSA groups (%)	
0-4.0 ng/ml	28 (7.6)
4.1-10.0 ng/ml	139 (37.9)
10.1-20.0 ng/ml	133 (36.2)
> 20 ng/ml	67 (18.3)
Neoadjuvant treatment	48 (13.1)
Adjuvant radiotherapy	97 (26.4)

Table 1. Characteristics of patients with clinically localized prostate cancer

Results

Our distribution of pT2, pT3 and pN positive patients by Gleason scores is shown in Table 2 and

	pT1-2	(%)	pT 3	(%)	p N +	(%)
G2-4 No=49	44	(89.8)	4	(8.2)	1	(2.0)
G5-7 No =139	127	(58.2)	85	(39.0)	6	(2.8)
G8-10 No = 133	10	(19.2)	36	(69.2)	6	(11.6)

Table 2. Distribution of pT2, pT3 and pN positive patients by Gleason scores

	pT 2	(%)	pT 3	(%)	pN +	(%)
PSA 0-4 ng/ml No=28	23	(82.1)	5	(17.9)	0	(0)
PSA 4.1-10 ng/ml No =139	89	(64)	46	(33.1)	4	(2.9)
PSA 10.1-20 ng/ml No = 133	69	(52)	57	(42.2)	7	(5.2)
PSA > 20 ng/ml No = 67	29	(43.3)	32	(47.8)	6	(8.9)

Table 3. Distribution of pT2, pT3 and pN positive patients by PSA groups

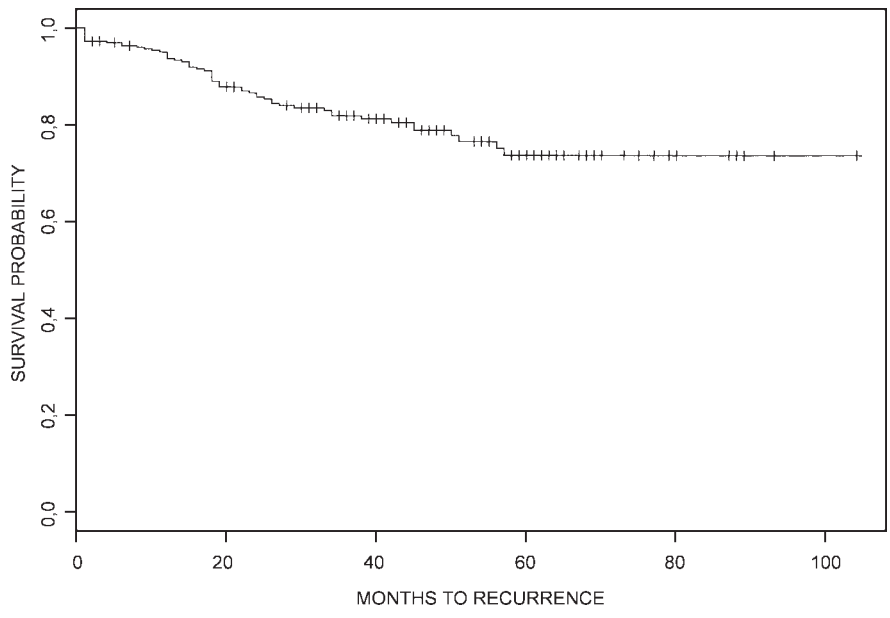

Fig. 1. Overall Kaplan-Meier survival (367 patients)

by PSA groups in Table 3. The overall 5-year biochemical failure-free survival value for our 367 patients was 73.9% (Fig.1) and the values for the pT2, pT3, and pTN positive groups were 78.8 %, 75.2 %, 17.3 %, respectively (p= 0.00025) (Fig. 2). The 5-year biochemical failure free survival values by Gleason scores G2-4, G5-7, G8-10 (Fig. 3) were 87.1%, 73.0%, and 55.3%, respectively (p=0.00016). The 5-year biochemical failure free survival values by classic PSA groups 0-4 ng/ml, 4.1-10 ng/ml, 10.1-20 ng/ml and

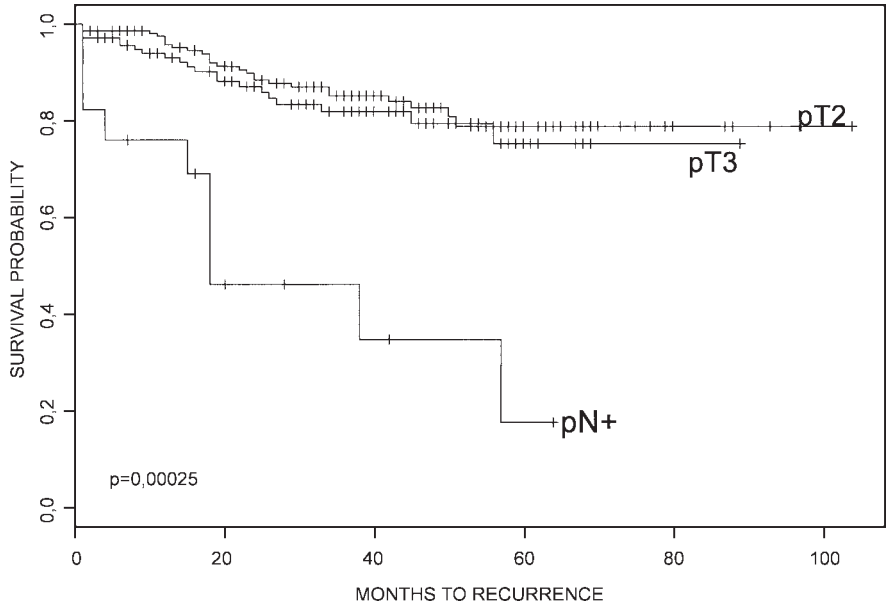

Fig. 2. Kaplan-Meier survival by pathologic stages (p=0.00025)

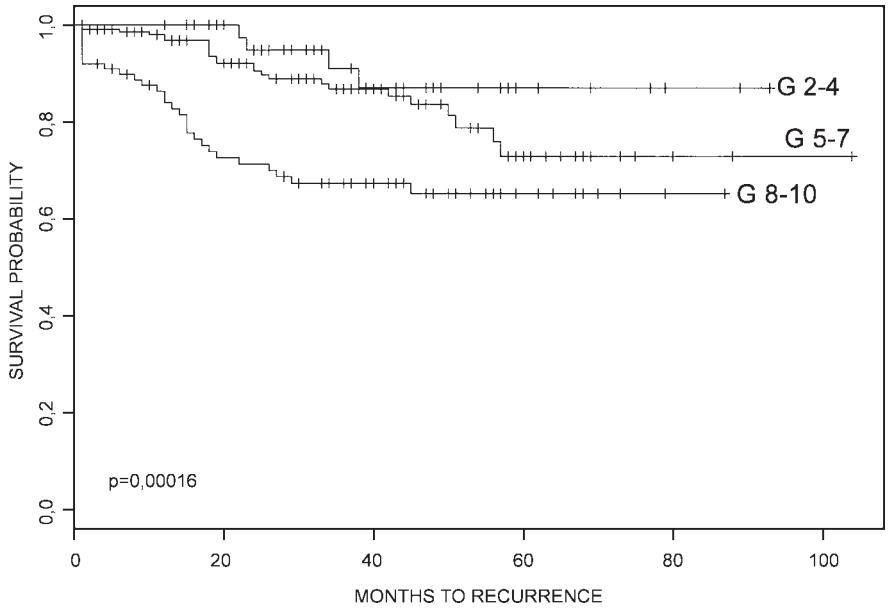

Fig. 3. Kaplan-Meir survival by histological Gleason score (p=0.00016)

greater than 20 ng/ml were 100%, 78.5%, 69.6% and 63.7% , respectively (p= 0.00029) (Fig.4). A summary of the patients that developed early complications is presented in Table 4, and compared with the complications reported by other centers such as Washington University, Mayo Clinic, Ulm, Toulouse and Baylor College (7). Using the Eastham classification (11) we determined that 74% of our patients had total urinary continence, 10% had urinary incontinence caused by stress, which did not require the use of diapers and 13.4% had moderate incontinence caused by stress, which required the use of diapers and 2.6 % had total urinary incontinence. We also determined that 10.4% had vesicourethral anastomotic stricture after their radical prostatectomy. In 167 of our (interviewed) patients, we determined that only 37.9% were potent, but many of the impotent patients resumed sexual activity with the use of vaso-active drugs or devices.

Discussion

The progress that has been made in the early detection of suitable patients has led to radical prostate surgery as the treatment of choice for the majority of urologists and its consideration as the gold standard for the treatment of clinically localized prostate cancer. Estimating the probability of curing a patient by radical prostatectomy is a goal of obvious

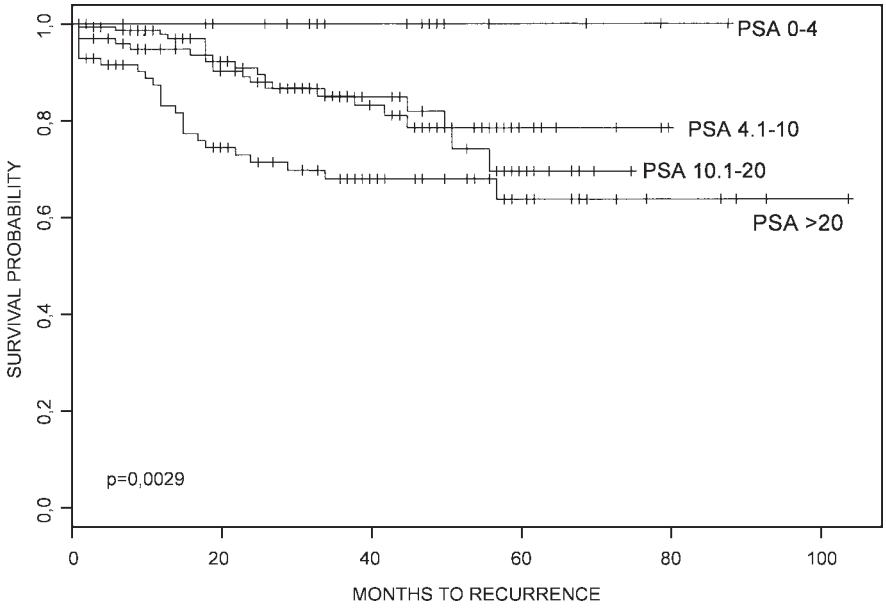

Fig. 4. Kaplan-Meir survival by PSA groups (p= 00029)

	Present study (%)	Other Centers (%)
Mortality	0.3	0.3
Pulmonary embolism	0.3	1.1
Myocardial infarction	0.3	0.6
Rectal injury	2.2	0.7
Vesicorectal fistula	0.3	0
Premature catheter loss	0.5	0.6
Lymphocele	0.5	0.4
Thrombophlebites/deep venous thrombosis	1	1.3

Table 4. Comparison of Mortality and Early Complications with overall results from large studies of several centers: Washington University, Mayo Clinic, Ulm, Toulouse and Baylor (7)

interest in order to ascertain the evolution of the disease and the need for additional treatment. Unfortunately the prognostic factors available to us are not sufficiently reliable for definitive conclusions. The most reliable indicators which are presently available are preoperative PSA level, pathological stage and Gleason histological grading system. From our experience with patients who have a clinically localized cancer, only 57.2% were found to be pathologically localized. This finding indicates a clinical understaging of 42.8%, and the difficulty we had, in selecting good surgical candidates. This proportion is not so different from that obtained by other authors (Fig. 5) (12, 13, 14, 15) and reflect their selection criteria. Our distribution of Gleason scores was also found to be within the range of those reported by others (Fig. 6) (16, 17, 14, 18). On the other hand, some researchers report higher percentage of radical prostatectomy in patients with lower PSA levels, and a smaller number of candidates with higher PSA levels (Fig. 7) (16, 17, 18, 19). These differences are probably due to the fact that our patients were not part of a planned screening study

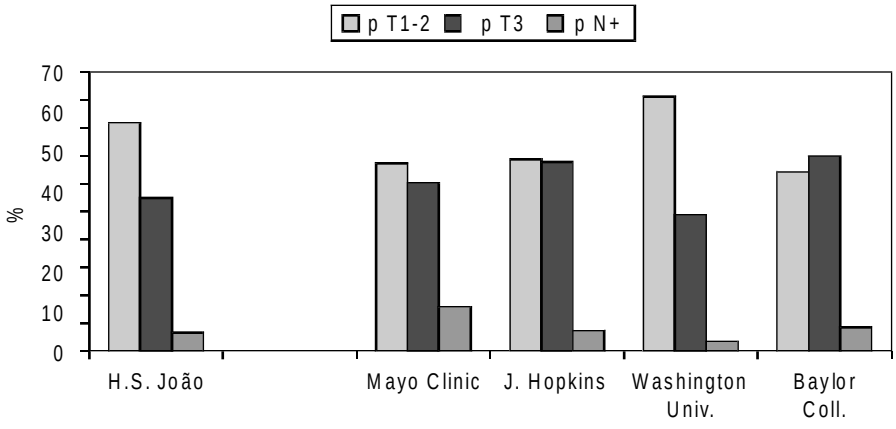

Fig. 5. Comparison of pathologic stage with the values presented by Mayo Clinic (12), Johns Hopkins (13), Washington University (14), and Baylor College of Medicine (15).

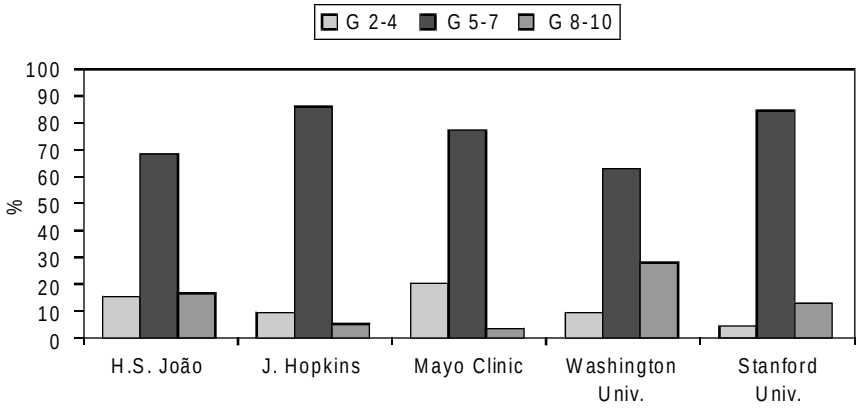

Fig. 6. Comparison of Gleason scores with values presented by Johns Hopkins (16), Mayo Clinic (17), Washington University (14) and UCLA (18).

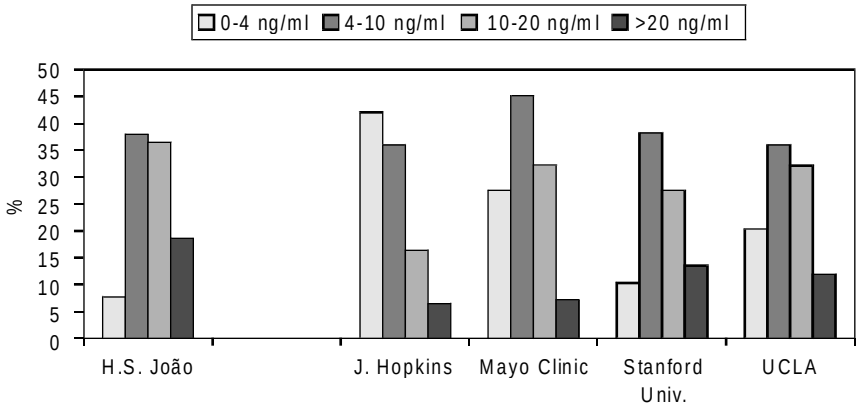

Fig. 7. Comparison of PSA groups with values presented by Johns Hopkins (16), Mayo Clinic (17), Stanford University (18) and UCLA (19).

and were chosen primarily on the basis of their laboratory and (or) clinical findings. Our overall 5-year biochemical failure-free survival was 73.9%, which is within the range of 70-83% found in the literature (7), but is somewhat lower than the range of 78-84% presented in various recent studies in world-renowned centers of reference showed in Table 5 (20). Our results could in the future become much better as the patient selection process improves and the number of patients and the follow up period increase. In this study we initially included patients with preoperative PSA levels up to 50 ng/ml. Since 1995 we have decreased the PSA cut-off value to 25 ng/ml at which patients were considered good candidates for surgery. The biochemical failure-free survival of 78.8 %, obtained for pathologically localized stages were lower than those found in other centers of reference (Table 6) (20). There are several reasons that may contribute to this lower value, such as the selection of surgical candidates and the processing method of the prostatectomy histological specimen. When we compare our survival rates based on Gleason score with the results from Baylor College of Medicine (15), our cancer patients with grades, G2-4 and G8-10 have lower survival rates of 97.1% versus 100%, and 65.3% versus 78%, respectively. Our patients with grades G5-7 have survival rates that are greater, 88.9% versus 80%. Our PSA groups survival results are not significantly different from those reported by others, given the higher initial PSA levels of our patients (Table 6). The rates of early complications exhibited by our patients are similar to those reported in other centers of reference, except for rectal injury and anastomotic stenosis (Table 4). This can be explained by presence, in our hospital, of physicians in training, learning several steps of the surgical technique.

Urinary incontinence remains one of the most troubling side effect following radical prostatectomy. In the literature, the reported rates of this complication vary widely, ranging from 5 to 31%, depending on the definition of incontinence and the manner in which it is determined by questioning the patient (7). The Baylor College of Medicine reports a continence rate of 92% during the first year, and 95% during the second year (20).

Our rate of social continence is 84%. The vesicourethral anastomotic stricture is a late complication, reported in the literature with an incidence ranging from 0.5 to 21% (21). Whereas the majority of complications appear to be diminishing, vesicourethral anastomotic stricture is still an inevitable problem in the majority of studies. The cause is unknown (21) but has been attributed to deficient

surgical technique, bladder mucosal eversion, mucosa-to-mucosa apposition, tension-free watertight vesicourethral anastomosis, urinary extravasation, prior transurethral surgery, microvascular disease, and predisposing factors like hypertension, cigarette smoking and diabetes mellitus (21, 22).

Impotence was the rule before the technical advances of Walsh (23). The actual rate of post-prostatectomy impotency ranges from 20% and 90%, depending on age, pathological stage and extent of the neurovascular bundle injury (7). Some authors have obtained percentages of potency of 32% when the two bundles were conserved, 13% when only one was conserved and 1% when no bundle was preserved (24). We have evaluated 167 patients with a personal interview and have found that 86.8% of these patients were potent prior to their operation. After surgery 37.9% were potent, a result similar to those reported by others (24). Many of these patients, who consider themselves impotent, returned to sexual activity with the support of various devices such as vacuum devices, implants, and vasoactive agents**.**

Conclusions

The results we obtained with radical prostatectomy show that it is a safe, and reasonable procedure, with reduced morbidity, in a hospital environment, which is outside the established world-renowned centers. Our data show that using a criterious clinical evaluation with standart prognostic factors, namely preoperative total PSA, better patient selection and a good surgical techniques is possible to obtain results which are similar to those from world-renowned hospitals

References

1. Damber JE, Prostate cancer: epidemiology and risk factors. Current Opinion, 8:375-380, 1998.
2. Internet, www.nci.nih.gov//NCI)
3. Dikman GA, Debruyne FMJ: Epidemiology of prostate cancer. Eur Urol, 30: 281-295, 1996.
4. Ekman P, Adolfsson J, Gronenberg H: The natural history of prostate Cancer. In: Prostate Cancer (Kaisary AV, Murphy GP, Denis L, Griffiths K, ed). London, Martin Dunitz Ltd 1999, pp 1-16.
5. Schoreder FH, Karnes R, Rietbergen J, Hoedemaeker R, Kirkel W, and members of the ERSPC, section Rotterdam, The european randomized study of screening for prostate cancer (ERSPC): An update. Eur Urol, 35: 539-543, 1999.
6. Dillioglugil O, Miles BJ, Scardino PT: Current controversies in the management of localized prostate cancer. Eur Urol, 28: 85-101, 1995.
7. Eastham JA, Scardino PT: Radical Prostatectomy; in Patrick C Walsh, Alan B Retik, E Darracott Vaughan, Alan J Wein (eds): Campbell's Urology 7th Ed. WB Saunders Company. Chap 85, pp 2547-2564.
8. Walsh PC: Anatomic radical retropubic prostatectomy; in Patrick C. Walsh, Alan B Retick, E Darracott Vaughan, Alan J Wein (eds). Campbell's Urology 7th Ed. WB Saunders Company. Chap 86, pp 2565-2588.
9. American Joint Committee on Cancer: Genitourinary cancer, prostate; in Manual for staging of cancer 4th Ed. Beahrs OH, Henson DE, Hutter RV, Kennedy BJ (eds.). Lippincott-Raven, Philadelphia,1992, pp 181-183.
10. Gleason DF: Classification of prostate carcinoma. Cancer Chemother Rev, 50: 125-128, 1996.
11. Eastham JA, Kattan MW, Rogers E, Goad JR, Ohori M, Boone TB, Scardino PT: Risk factors for urinary incontinence after radical prostatectomy. J Urol, 156:1707-1713, 1996.
12. Zincke H, Oesterling JE, Blute ML, Bergstralh EJ, Myers RP, Barret DM: Long-term results after radical prostatectomy for clinically localized (stage T2c or lower) prostate cancer. J Urol, 152: 1850-1857, 1994.
13. Walsh PC, Partin AW, Epstein JI: Cancer control and quality of life following anatomical radical retropubic prostatectomy: results at 10 years. J Urol, 152: 1831-1836, 1994.
14. Catalona WJ, Smith D: 5-year recurrence rates after anatomical radical retropubic prostatecomy for prostate cancer. J Urol, 152: 1837-1842, 1994.
15. Dillioglugil O, Leibman BD, Kattan MW, Seale-Hawkins C, Wheeler TM, Scardino PT: Hazar rates for progression after radical prostatectomy for clinically localized prostate cancer. Urology, 50:93-99, 1997.
16. Partin AW, Yoo J, Carter HB, Pearson JD, Chan DW, Epstein JI, Walsh PC, The use of prostate specific antigen, clinical stage and Gleason score to predict pathological stage in men with localized prostate cancer. J Urol, 150: 110-114, 1993.
17. Lerner SE, Blute ML, Bergstralh EJ, Bostwick DG, Eickolt JT, Zincke H, Analysis of risk factors for progression in patients with pathologically confined prostate cancers after radical retropubic prostatectomy. J Urol, 156: 137-143, 1996.
18. Smitt M, Heltzrl M, The results of radical prostatectomy at a community Hospital during the prostate specific antigen era. Cancer, 77: 928-933, 1996.
19. Trapasso JG, deKernion JB, Smith RB, Dorey F: The incidence and significance of detectable levels of serum prostate specific antigen after radical prostatectomy. J Urol, 152: 1821-1825, 1994.
20. Murphy G, Khoury S, Partin A, Denis L (edt): Prostate Cancer. 2nd International Consultation on Prostate Cancer, Paris, June, 27-29, pp 271-282, 1999.
21. W Tomshi, G Suster, W Holtl: Bladder neck strictures after radical prostatectomy: still an unsolved problem. British J Urol, 81: 823-826, 1998.
22. Boboroglu PG, Sand JP, Roberts JL, Amling CL: Risk factors for vesicourethral anastomotic stricture after radical prostatectomy. Urology, 56:96-100, 2000.
23. Walsh PC, Mostwin JL: Radical Prostatectomy and Cystoprostatectomy with Preservation of Potency. Results Using a New Nerve-sparing Technique. British J Urol, 56: 649-697, 1984.
24. Cespedes RD, Swanson DA: Complications of radical prostatectomy; in: Martin I. Resnick, Ian M. Thompson (eds): Surgery of Prostate. Churchill Livingston, Chap 9, pp 181-195, 1998.