

PROSPECTIVE ANALYSIS OF THE BIOCHEMICAL RECURRENCE OF PROSTATE CARCINOMA AFTER PRESERVATION OF THE BLADDER NECK IN RADICAL PROSTATECTOMY

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ABSTRACT

Objectives: The preservation of the bladder neck in radical prostatectomy has been supported in literature as an important step in the urinary continence maintenance. In this prospective study a comparison was made of the urinary continence rates and neoplasm control based on preservation or resection of the bladder neck.

Material and Methods: Patients with stage T1c – T2c prostate adenocarcinoma treated by radical prostatectomy, were randomized during the surgery, by drawing, either for the bladder neck preservation or for resection. The continence was evaluated in an interview 2 days after the Foley catheter removal and in the second and sixth months after the surgery. The same pathologist examined the surgical margins systematically. The neoplasm control was assessed by prostate specific antigen (PSA) dosage in the second month after the surgery and later, semiannually.

Results: An interim analysis of the first 70 patients, showed a high incidence of exclusively involvement of the bladder neck surgical margin in the preservation group and, due to this finding, the study was closed prematurely. Each group was assigned 35 patients but the bladder neck could not be preserved in 4 and 1 died, leaving 31 in the preservation group and 38 in the resection group. There was no statistical difference between the 2 groups as to the early or late urinary incontinence rates. Two days after the catheter removal and in the second and sixth months after the surgery the respective rates were: 21%, 13% e 5% in the bladder neck resection group and 32%, 13% e 3% in the bladder neck preservation group. The PSA dosage showed a biochemical recurrence of the neoplasm (> 0.3 ng/ml) in six of the 30 (20%) patients submitted to bladder neck preservation and in five of the 33 (15.15%) patients submitted to bladder neck resection, after a median of 27 months of follow-up (25 to 30 months). The difference between the two groups was not statistically significant ($p = 0.74$).

Conclusions: The bladder neck preservation in radical prostatectomy does not improve the postoperative continence rates, shows a tendency to produce more positive surgical margins at the bladder neck level, but the neoplasm evolution is not different when compared to patients submitted to bladder neck resection.

Key words: prostate; prostatic neoplasia; prostatectomy; urinary incontinence

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INTRODUCTION

The increase of prostate cancer detection in initial stages (T1 – T2) resulted in a significant increase in the number of radical prostatectomies. Having as objective the decrease of morbidity related to the surgical procedure, many researchers are

studying procedures to refine the prostatectomy technique, but always with the concern of not compromising the neoplasm cure.

The radical prostatectomy is a procedure associated to undesirable outcome such as sexual impotence and urinary incontinence. The pioneering studies of Walsh et al.(1) described precisely the

pelvic anatomy of man and allowed for a surgery performed with smaller risks of sexual impotence and urinary incontinence, more acceptable by the patients. The surgical technique described by Walsh includes the bladder neck resection with the prostate and the seminal vesicles. The author reports that 91% of the treated patients remain continent and do not use any urinary pad (2).

Moderate or pronounced urinary incontinence is seen in 2% to 40% (3-6) of the patients submitted to radical prostatectomy. The lower rates are seen in those operated by teams that have greater experience with the surgical technique. The mechanism of continence after prostatectomy has been studied and there are two functionally independent anatomical structures involved in this mechanism: the external or distal sphincter and the internal or proximal sphincter, in the bladder neck.

Several attempts to improve continence rates after radical prostatectomy, sparing these anatomical structures have been reported: bladder neck preservation (7,8); bladder neck tubularization (9,10); puboprostatic ligaments sparing (11) and careful dissection of the urethra sparing the striated sphincter (12).

The bladder neck preservation has been supported as an important maneuver in the urinary continence maintenance, without compromising the patients cure rate (7,8).

This randomized, controlled, double-blind study of patients with a localized prostate cancer diagnosis was performed to evaluate prospectively the results of the bladder neck preservation in radical prostatectomies in what concerns the urinary continence rates, tumor free surgical margins and the neoplasm control.

MATERIAL AND METHODS

Participants: All the patients with clinical diagnosis of prostate adenocarcinoma T1 and T2 who were candidates to radical prostatectomy in this institution, from May to October 1998, participated in this study. Patients with a previous history of prostate transurethral resection and those with

neurogenic dysfunction of the lower urinary tract were excluded. Two patients stage T3a who were considered borderline between T2 and T3 were included. All patients were clinically staged using the TNM classification (13). For this purpose, the patients were analyzed through digital rectal exam, prostate specific antigen and total and prostate acid phosphatases dosages in the serum, bone scan, computerized tomography of the abdomen and chest X-ray. At the end of the evaluation, forty patients had the disease stage T1c (57%), thirteen, stage T2a (18%), eight, stage T2b (12%), seven, stage T2c (10%) and two patients, stage T3a (3%).

The study was planned to have with 120 patients with prostate adenocarcinoma, stages T1 – T3a. This to have a power of 80% in the detection of a difference of 15% in the urinary incontinence rates between the groups; but, at the end, 70 patients were evaluated and included in the study due to ethical reasons. The interim analysis of the results showed a high frequency of positive margins exclusively at the bladder neck level in the bladder neck preservation group and the study was interrupted.

Surgery: All patients were submitted to radical prostatectomy by the same surgeon (MS), according to a technique previously published (14), preserving the maximum of the distal sphincter complex. Drawing, during the surgery made the decision of preserving or resecting the bladder neck. The bladder neck preservation technique was described by Malizia et al. (7) and the bladder neck resection technique was described by Walsh et al. (1).

Histopathological study: All specimens were prepared and analyzed by the same pathologist (KRL). The surgical specimens were fixed in 10% buffered formaldehyde, for a period of four to sixteen hours. The whole gland was analyzed histologically according to methods previously described (15). The whole gland was included in the exam after its margins were stained with India ink.

For the histologic study the specimens were treated as usual with dehydration in alcohol and clarification in xylol, followed by inclusion in paraffin. Cuts of 4 a 6 μ m were stained with hematoxylin and eosin and analyzed in a light microscope.

The histopathological study of the surgical specimen included the assessment of the Gleason score (16), tumor volume (17) and surgical margins. Margins were considered positive when infiltrate tumor was found in the thin cuts in the prostate apex and in the bladder neck as well as when the tumor was interrupted at the borders stained with India ink.

Criteria for evaluation: After the Foley catheter removal, on the fourteenth postoperative day, the patients of both groups were evaluated as to urinary continence in the following periods: 48 hours, two months and six months. Urinary incontinence was defined as the need to use more than one pad per day. Besides, immediate postoperative complications (up to the thirtieth postoperative day) and delayed (between the first and the sixth postoperative months) were recorded, including urinary fistulas and bladder neck strictures. The same researcher (LJN) interviewed the patients, and he had no knowledge about the type of procedure that the patient had had.

To assess the surgery efficiency in what concerns the tumor removal, the incidences of positive margins in both groups were compared, emphasizing the study of the bladder neck.

The neoplasm postoperative control was performed by dosage of specific prostate antigen, total and prostate acid phosphatases in the serum and digital rectal exam in the second month and at every six months after the first dosage as well as yearly bone scan and chest radiography.

Statistical analysis: To analyze the characteristics of both groups the Chi-square test was used to

compare age, stage, PSA and Gleason score. The Fisher exact test was used to compare the results of continence at two and six months, in the histopathological analysis and in the neoplasm biochemical recurrence analysis. The Chi-square test was used to analyze the results of continence in 48 hours. To reject the hypothesis of nullity the critical level $\alpha = 5\%$ ($p = 0.05$) was considered.

RESULTS

Patients characteristics: The age of the patients ranged from 46 to 74 years (median = 62.5), 68 were Caucasian and two, Asiatic. Thirty-five patients were initially allocated to the bladder neck preservation group and the other 35 were submitted to bladder neck resection. In four of the 35 patients of the preservation group it was not possible to spare the neck because the median lobe was enlarged. These patients were included in the bladder neck resection group, then with 39 patients. One patient died in the thirteenth postoperative day due to a pulmonary embolism. The final groups had 38 patients in the bladder neck resection group and 31 in the bladder neck preservation group. Both groups were comparable as to age, stage, PSA and Gleason score (Table-1).

Urinary continence: Among the 38 patients submitted to bladder neck resection, eight (21%) reported urinary incontinence 48 hours after the Foley catheter removal, 5 (13%) after two months and 2

Table 1 - Patients characteristics in each experimental group.

		Bladder Neck Preservation	Bladder Neck Resection	p
Age	< 65	20	25	0.97
	> 65	11	14	
Stage	T1c – T2a	26	27	0.16
	T2b – T2c	5	12	
PSA	< 10	21	26	0.92
	> 10	10	13	
Gleason	2 – 6	22	26	0.70
	7 – 10	9	13	

(5%) after 6 months. Among the patients who had the bladder neck spared, urinary incontinence was seen in 31 patients (33%) after 48 hours, four (13%) after two months and one (3%) after 6 months. As to urinary incontinence there was no statistically significant difference between the two groups at any time.

Surgical Margins: The pathological evaluation of the surgical specimens showed positive margins at the bladder neck level in six of the 70 patients (8%), with involvement by the neoplasm only in the bladder neck in three of the 31 patients (10%) in whom these structures were spared. In none of the patients submitted to bladder neck resection was bladder neck involvement seen. Positive surgical margins were seen in other sites and bladder neck in one patient of the preservation group and in two patients of the resection group. Although there was a greater incidence of positive margins only in the preservation group bladder neck, the figures showed no statistically significant difference ($p = 0.082$).

Biochemical recurrence: The specific prostate antigen dosage showed biochemical recurrence of the neoplasm (> 0.3 ng/ml) in 6 (20%) of the 30 patients submitted to bladder neck preservation and in 5 (15.15%) of the 33 submitted to bladder neck resection (Table-2), after a median of 27 months of follow-up (25 to 30 months). The difference between the 2 groups was not statistically significant ($p = 0.74$). Adjuvant androgen suppressive therapy was introduced for 3 of the 30 patients of the preservation group and for three of the 33 patients submitted to bladder neck resection because they showed a high-risk histopathological study (Gleason > 8 or involvement of the seminal vesicle by the neoplasm). Raised PSA was seen in all patients with involvement of the surgical margin at the bladder neck level.

DISCUSSION

Although in this study no urinary continence improvement was seen with the e bladder neck preservation, other authors have shown that sparing the bladder neck during radical prostatectomy, improves urinary continence in the postoperative. Malizia et al. (7) reported 100% of early urinary continence and adequate surgical margins in 20 patients submitted to radical prostatectomy with bladder neck preservation. Shelfo et al. (8) studied retrospectively 365 patients submitted to the same technique, and have found 88% of urinary continence. Even though they have found 32% of involved surgical margins, they emphasized that the bladder was the only site involved in just 0.5% of the cases. They concluded that the bladder neck sparing in prostatectomy does not alter the chances of cure and improves the urinary continence rates when compared to historical controls. In a prospective and sequential study, Lowe (18) performed prostatectomy with bladder neck resection in 99 patients in the first year and, in the next year, 91 patients had the bladder neck preserved. There was total continence after one month and one year, respectively, in 11.2% and 86.3% in the resection group and in 23.3% and 89.4% in the preservation group. According to him, the bladder neck sparing could not be carried out in 15% of the planned cases due to technical difficulties. He concluded that urinary continence returns faster in the patients with bladder neck preservation but this difference disappears nine months after the surgery. Gaker et al.(19) have seen more favorable rates of early continence in the bladder neck preservation and they state that this maneuver prevents the anastomotic strictures that would compromise the continence.

Table 2 - Incidence of biochemical recurrence in the experimental groups.

	Preservation	Resection	Total	p
Recurrence (PSA > 0.3)	6 / 30 (20%)	5 / 33 (15.15%)	11 / 63 (17.46%)	0.744
Hormone	3 / 30 (10%)	3 / 33 (9.09%)	3 / 63 (9.52%)	0.999

On the other hand, Licht et al. (20) evaluated, prospectively, 206 patients submitted to radical prostatectomy with bladder neck preservation and concluded that there is no improvement in urinary continence with the preservation, yet this maneuver is associated to a smaller chance of the vesico-urethral anastomosis stricture. They found 7% of positive margins in the bladder neck and this fact is related to great volume tumors and extra-prostate involvement.

Recently, Kaye et al. (21) evaluated the bladder neck preservation technique associated to three types of prostate apex dissection: “sphincter damaging” (ligature and section of the dorsal vein complex); “sphincter repairing” (the venous complex as part of the striated sphincter is incorporated in the anastomoses); and “sphincter preserving” Myers technique (22). The continence rates were of 90%, 93% and 97% and the average time for its recovery was of 100, 52 and 30 days with the first, second and third techniques, respectively, thus proving the importance of the external sphincter preservation in the early return of continence.

In this study all patients were operated preserving at most the integrity of the distal sphincter complex. Continence was obtained 48 hours after the Foley catheter removal in 67% of the patients with bladder neck preservation and in 79% of the patients who had resection. After 2 months both groups presented continence rates of 87%, without any statistical difference between the 2 groups. This showed that the urinary continence after radical prostatectomy depends on the distal sphincter mechanism.

During this study an interim analysis showed involvement of the surgical margin exclusively at the bladder neck level in 10% of the patients submitted to this structure sparing and in none of the cases where the bladder neck was resected. Epstein et al. (23) assessed the clinical impact of positive surgical margin after prostatectomy. In 47% of the cases with positive margins there was a progression of the disease while in the patients with negative margins, progression was seen in 18% of the cases. This fact led to the interruption of the study, as no greater continence rate was seen with the bladder neck preservation and at the same time there was a greater

incidence of positive margins exclusively in the bladder neck in this group. In a previous study, we compared bladder neck preservation and resection in a randomized trial, looking at continence rates and surgical cancer controls (24). It must be emphasized that in this previous study (24), we found that a difference of positive surgical margins at the bladder neck level did not reach statistical significance, but the value of “p” was near to the significance level ($p = 0.082$). This number suggests that the bladder neck preservation technique has a tendency to produce more positive margins at the bladder neck level and this tendency might reach a statistical significance if a greater number of patients were to be studied in each group. Due to ethical reasons this hypothesis could not be explored.

The delayed postoperative analysis (27 months) of the experimental groups showed that all the patients who had positive margins in the bladder neck evolved with increase of PSA, proving that a positive surgical margin is followed by high rates of neoplasm recurrence. On the other hand, it was seen that the increase of PSA was the equivalent in both groups ($p = 0.74$), probably due to other variables of the neoplasm that act as factors of progression, besides the involvement of the bladder neck.

CONCLUSION

The bladder neck preservation in radical prostatectomies does not improve the postoperative continence rates, tends to produce more positive surgical margins at the bladder neck level, but the neoplasm evolution shows no difference when compared to patients submitted to bladder neck resection.

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