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UROLOGICAL ONCOLOGY

A surveillance schedule for G1Ta bladder cancer allowing efficient use of check cystoscopy and safe discharge at 5 years based on a 25-year prospective database

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Purpose: In the absence of clear evidence, surveillance of low-grade superficial bladder cancer by regular check cystoscopy may continue unnecessarily, or discharge from follow-up may occur empirically. We review the follow-up during a prospective 25-year period of patients presenting with G1Ta bladder cancer, and it is this analysis on which we base a safe schedule for discharge.

Materials and Methods: A prospectively kept, computerized record of bladder cancers diagnosed between 1978 and 1985 and subsequently followed up at the Western General Hospital, Edinburgh was reviewed.

Results: A total of 115 patients with G1Ta disease were followed for a mean of 19.4 years. Tumor status at 3 months was the strongest prognostic factor for recurrence. Although the absence of tumor at 1 year was also a favorable prognostic sign, it was not for 5 years that the situation entirely stabilized (recurrence developed in 8 of 66 such patients between 1 and 5 years). Of those who did not have recurrence in 5 years, 98.3% patients remained tumor-free for 20 years. In contrast in those with recurrence at 3 months the recurrence rate was much higher. Overall 12% of patients experienced progression, mostly in year 1. None of the 8 who had their first recurrence after year 1 had disease progression.

Conclusions: Patients with G1Ta disease who are free of recurrence for 5 years after presentation can be safely discharged. We propose to alter the regime for patients with no recurrence in year 1 and discharge them at 5 years.

Editorial Comment

The surveillance schedule of superficial bladder cancer is empirical and based upon convenience rather than biological data. In recent times, attention has been focused on modifying the strict schedule of 3-monthly cystoscopies in certain risk groups. This paper focuses on pTa G1 cancer and bears some very interesting data. First, multiple and/or large tumors have a significantly higher risk for recurrence. Second, the first 5five years after TUR are important, with overall recurrence rates dropping from 29.1% to 14.1% ($p = 0.009$). Third, recurrence at 3three months is a bad prognostic sign. Patients who had recurrence at 3 months had further recurrences at 1 year compared with those who were tumor-free at 3 months (55.5% vs. 17.8%, $p = 0.007$). Progression occurs even in these tumors. 12.2 % had progression, which is an unexpected high figure to my opinion. 50% progressed within the first 5 years, and 35.7% within 3 months. All these patients had multiple primaries. 85.7 % of these patients had recurrence at 3 months.

Two consequences can be drawn from this important contribution. First, without recurrence, follow-up can be terminated at 5 years. Second, even TaG1 tumors sometimes recur aggressively and may progress.

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The extent of lymphadenectomy for pTXNO prostate cancer does not affect prostate cancer outcome in the prostate specific antigen era

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Purpose: Recent data suggest that extended lymph node dissection in prostate cancer may be necessary for accurate staging. With limited lymph node dissection apparently node negative cases might be under staged. We determined the impact that the number of lymph nodes removed at radical retropubic prostatectomy (RRP) has on cancer progression and cause specific survival in pTXNO cases.

Materials and Methods: We reviewed the RRP prostate cancer database on 7,036 patients with clinical T1 to T3 disease, no adjuvant therapy and node negative disease in the prostate specific antigen (PSA) era from 1987 to 2000. Factors evaluated were the number of lymph nodes obtained at RRP, preoperative PSA, clinical and pathological stage and grade, margin status, year of surgery and specific surgeon for 5 surgeons who operated throughout the period and performed more than 500 RRPs. Cox analysis was done to determine the RR of progression (PSA or systemic) and prostate cancer death for the number of lymph nodes excised.

Results: Median patient age was 65 years and median preoperative PSA was 6.6 ng/ml. At pathological evaluation 5,379 tumors (77%) were organ confined, 4,491 (65%) were Gleason score 5 to 6 and 2,027 (29%) were Gleason score 7 to 10. The median number of nodes obtained significantly decreased from 14 in 1987 to 1989 to 5 in 1999 to 2000 ($p < 0.001$). Ten years after RRP Kaplan-Meier estimates were 63% of cases free of PSA progression, 95% free of systemic progression and 98% free of prostate cancer related death. Median follow-up was 5.9 years. After adjusting for pathological factors (PSA, grade, stage, margin status and surgical date) the number of lymph nodes obtained at lymphadenectomy was not significantly associated with PSA progression (for each additional node (RR 0.99, 95% CI 0.98 to 1.02, $p = 0.90$), systemic progression (RR 0.99, 95% CI 0.96 to 1.03, $p = 0.68$) or cause specific survival (RR 1.01, 95% CI 0.96 to 1.06, $p = 0.75$).

Conclusions: The extent of lymphadenectomy does not appear to affect prostate cancer outcome in lymph node negative cases. This includes patients with high preoperative PSA, high pathological grade and extracapsular disease. These results suggest that under staging is not present in apparently node negative cases with limited lymphadenectomy and, even if present, its impact on outcome is likely to be negligible.

Editorial Comment

The extent of lymphadenectomy at radical retropubic prostatectomy (RRP) is controversial. The authors analyze their results in 7,036 patients. Ten years after RRP 63% of patients remain free of progression according to Kaplan-Meier estimates. Briefly, this paper shows clearly that in N0 patients no progression or survival

advantage exists with an increased number of nodes excised, including a group with high-risk cancer. Controversial data from European centers may be due to more advanced disease.

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FEMALE UROLOGY

Increased warning time with darifenacin: a new concept in the management of urinary urgency

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Purpose: We assessed the effect of darifenacin, an M3 selective receptor antagonist, on the warning time associated with urinary urgency.

Materials and Methods: In this multicenter, double-blind study subjects with urinary urgency for 6 months or greater and episodes of urgency 4 times or greater daily were randomized to darifenacin controlled release tablets (30 mg once daily) or placebo. Warning time was defined as the time from the first sensation of urgency to voluntary micturition or incontinence. Data were collected using electronic event recorders during 6-hour clinic visits or 3 urge-void cycles, if shorter, at baseline and at treatment end.

Results: A total of 72 subjects entered the study and 67 were included in the primary efficacy analysis (darifenacin in 32 and placebo in 35). Darifenacin treatment resulted in a significant increase in mean warning time with a median increase of 4.3 minutes compared with placebo ($p = 0.003$). Overall 47% of darifenacin treated subjects compared with 20% receiving placebo achieved a 30% increase or greater in mean warning time (OR 5.6, $p = 0.009$). Median and minimum warning times were also significantly increased following darifenacin treatment vs. placebo ($p = 0.004$ and 0.017, respectively). The median difference in minimum warning time was 1.9 minutes in favor of darifenacin vs. placebo.

Conclusions: To our knowledge this is the first study to evaluate change in warning time, which is potentially important to individuals with symptoms associated with overactive bladder. Darifenacin increases mean, median and minimum warning time compared with placebo, allowing subjects more time to reach a toilet and potentially avoiding the embarrassing experience of incontinence.

Editorial Comment

The authors analyze the efficacy of darifenacin, a selective M3 receptor antagonist, with regard to the parameter of micturitional warning time. Warning time was defined as the point from first sensation of urinary urgency to the patient voluntarily voiding or experiencing episode of urinary urge incontinence. The authors found that darifenacin affected a significant increase in warning time over those patients treated with placebo.

This is an excellent paper from one of the world's top urogynecologists. The analysis of warning time may produce a new benchmark of efficacy for OAB medications. This parameter, as it finds its way in use in more and more studies, will evolve. Currently, it is judged as the time between first sensation of urgency to the point of voluntary micturition or incontinence. Since voluntary micturition is a volitional act and urinary