Pattern of Recurrence Changes in Noninvasive Bladder Tumors Observed During 2 Decades

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Purpose: Previously published data on the 25-year outcome of G1Ta and G2Ta bladder tumors demonstrated that both tumors have a similarly low risk of recurrence in cases in which no tumor was detected in the first 5 years after presentation. A further 4 prospectively maintained cohorts were available for comparison between institutions or across time periods.
Materials and Methods: Review of a prospectively kept, computerized record of patients with bladder cancer allowed analysis of the long-term outcome of 4 further cohorts of bladder cancer presenting in 1978 to 1986 or 1991 to 1996.
Results: A total of 325 patients with G1Ta and 190 with G2Ta bladder tumors had up to 25 years of followup. The risk of recurrence in the first 5 years was identical in all cohorts from the 1980s. However, in those patients without recurrence in the initial 5 years, the subsequent risk of recurrence (in G1 and G2Ta tumors) was 3.2% in the earlier cohorts but increased 3-fold to 10.8% in the cohorts from the early 1990s (RR 3.3, 95% CI 1.2–9.5, p = 0.016).
Conclusions: A difference was observed in the pattern of late biopsy proven recurrence in the more contemporary cases. Increased use of prophylactic intravesical chemotherapy does not seem to be a strong factor. Changes in the ability to detect lesions and the readiness to biopsy suspicious lesions may be responsible for this difference.

Key Words: bladder neoplasms, risk assessment, recurrence, neoplasm staging

Low and moderate grade superficial transitional cell tumors, despite their almost benign nature, still require regular followup. However, the duration of this surveillance has not been clearly established. Authors presenting life table analysis advocate lifelong followup because recurrences were found to occur beyond 10 years.[1,2] Conversely, the European Association of Urology recommends discharging patients with G1Ta tumors if recurrence-free for 5 years.[3] This regimen is further substantiated by a recent postal survey of urologists in the southwest United Kingdom, in which 88% would discharge patients with a 5-year tumor-free period.[4]

Results from a prospective 25-year followup at our institution concluded that the risk of recurrence for a patient presenting with G1Ta tumor who remains tumor-free for 5 years is negligible thereafter and that these patients can be safely discharged at 5 years.[5] Similar recurrence patterns were observed for G1Ta and G2Ta bladder tumors.[6]

Access to a large database, prospectively kept and maintained for 25 years, has allowed us in this study to validate the previously published recurrence trends in cohorts of patients initially treated at another institution during a similar time frame (diagnosed between 1978 and 1986), as well as in a more contemporary cohort of G1Ta and G2Ta diagnosed between 1991 and 1996.

MATERIALS AND METHODS

From 1978 all patients presenting at our institution with bladder cancer were reviewed at a weekly clinicopathological meeting specifically for bladder cancer. Details of their presentations and subsequent progress were recorded prospectively. Lifelong followup was advocated, and there was widespread consensus and adherence to the protocols in use.

The WHO (1973) grading system and the UICC TNM 1978 system were used to characterize the tumors.[7] Until 1991 patients were treated in separate urological departments within Edinburgh—Western General Hospital and the Royal Infirmary of Edinburgh. Both urology units merged in 1991 and followup has since continued at the WGH.

This merging allowed examination of 6 separate cohorts. The groups were divided as 1—G1Ta (WGH 1978 to 1986) and 2—G2Ta (WGH 1978 to 1986), both previously reported upon,[5,6] 3—G1Ta (RIE 1978 to 1986) and 4—G2Ta (RIE 1978 to 1986) to validate the previous findings (fig. 1). These 4 cohorts contributed to the mitomycin Medical Research Council trials in the 1980s.[8] To form a comparison with more contemporary series we used 2 cohorts of patients diagnosed between 1991 and 1996, 5—G1Ta (WGH 1991 to 1996) and 6—G2Ta (WGH 1991 to 1996). Simultaneous upper tract involvement and carcinoma in situ precluded entry to the

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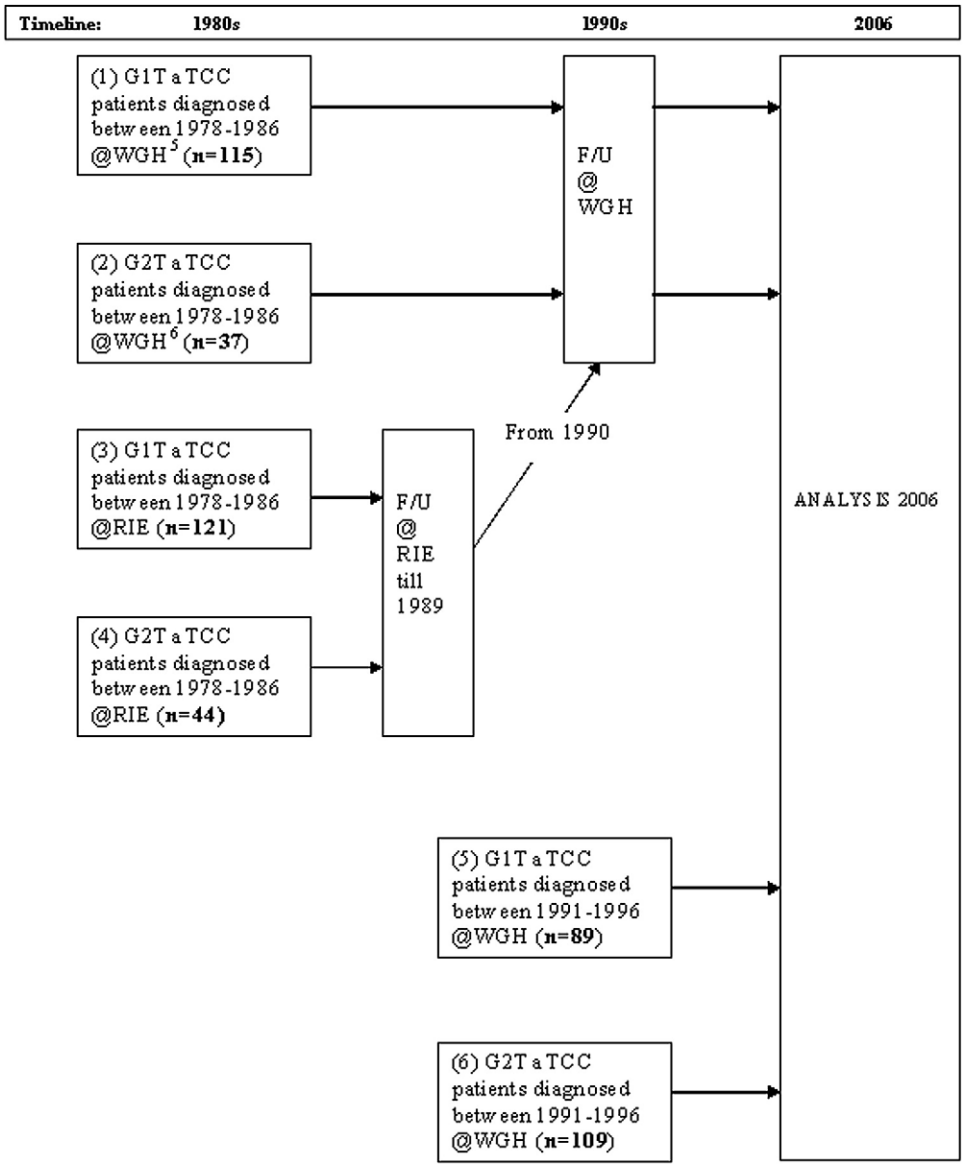

FIG. 1. Flow chart representing cohorts analyzed and published previously (1 and 2), and currently analyzed validation cohorts (3, 4, 5 and 6)

original cohorts and analysis in this study. The RIE validation cohorts (3 and 4) were reviewed independently by an author (ADGL) who was blinded to previous findings.

Followup of patients before 1990 was by general anesthetic cystoscopy commencing at 3 months after primary treatment, which was transurethral resection of bladder tumor or biopsy and diathermy. General anesthesia was regularly used for cystoscopy before 1986, and followup at that time included cystoscopy at 3, 6, 9 and 12 months before annual followup for those remaining tumor-free. Flexible cystoscopy was only used from 1986 onward. Recurrence was defined as a new, histopathologically confirmed TCC, occurring after primary treatment. All suspicious lesions and tumors were biopsied before definitive treatment. Recurrences were managed with TURBT or B&D. Progression was defined as a recurrent tumor with a grade or stage (pTNM) higher than G1pTa or G2pTa respective to the primary pathology. Histopathology slides of recurrences and suspicious lesions were rechecked by 1 uropathologist (KMG) if pathology documentation was unclear. In terms of statistical analysis, the Mantel-Haenszel and Fisher exact tests were used for significance testing where appropriate.

RESULTS

A total of 515 patients with G1 and G2Ta within 6 cohorts were reviewed. Of these, 236 G1Ta and 81G2Ta were diagnosed between 1978 and 1986, and 89 G1Ta and 109 G2Ta bladder tumors between 1991 and 1996. Patient and tumor demographics are detailed in table 1. A greater proportion of women was evident in the 1990s. There was a 2-fold increase in the use of MMC following primary treatment in the later cohorts (7.6% in the 1980s vs 15.3% in the 1990s, RR 2, 95% CI 1.2–3.3, $p = 0.04$). In all the cohorts the risk of recurrence at 3 months was higher for those with multifocal disease. Tumor evident at 3 months was consistently the strongest predictor of recurrence thereafter (RR 5.6, 95% CI 2.1–14.8, $p < 0.0001$).

Figures 2 through 7 display subsequent recurrence for the 6 cohorts. In those patients with tumor evident at

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