

Substaging T1 disease (Recommended)

Reason/Evidentiary Support

There have been many efforts to establish the optimum method of identifying T1 tumours with low and high risk for recurrence, progression and death from bladder cancer. One focus of many of these reports has been to “substage” T1 tumours. The two methods most used can be divided into quantitative and anatomical.

The largest volume of literature has tried to use the muscularis mucosae (MM) as a landmark to subdivide T1 tumours into 2 or 3 subgroups. The first study of this type is the report of Younes et al who divided tumours into T1a (invasion superficial to MM), T1b (to the MM) and T1c (deep to the MM).¹ They found that the T1b/T1c tumours were associated with a worse progression free and cancer specific survival. Since that report numerous groups have reported their experience with this approach.¹ The largest study to date is that of Rouprêt et al (2013) that evaluated 587 cases from multiple institutions in France.² On multivariable analysis, pT1b (involving or deep to MM) tumours had a significantly worse recurrence-, progression and cancer specific survival.² These authors also provide a comprehensive literature review that included 21 prior publications.² Based on this review a few observations can be made: (i) the ability to assess MM ranged from 58% to 100% (ii) on univariate analysis use of MM was a significant predictor of recurrence free survival in 4/12 reports, progression free survival in 15/17 reports and of cancer specific survival in 4 of 7 reports and (iii) on multivariable analysis it was significant for recurrence free survival in 3/12, for progression free survival in 13/16 and for cancer specific survival in 3/6 publications.² Additional studies have been published subsequently.³⁻⁵ The study by Orsola et al (2015) is significant in that this is a prospective study that used substaging based on invasion superficial to the MM (T1a) versus involving or deep to MM (T1b) to stratify patient treatment.⁵ The publication reports on the first 200 patients entered into the protocol.⁵ Although the follow up is limited in this initial report, substage was a highly significant predictor of tumour progression on multivariable analysis.⁵ These authors concluded: “In HGT1 bladder cancer, the strategy of performing a second TUR only in T1b cases results in a global low progression rate of 15.5%. Tumours deeply invading the lamina propria (HGT1b) showed a three-fold increase in risk of progression. Substaging should be routinely evaluated, with HGT1b cases being thoroughly evaluated for cystectomy. Inclusion in the TNM system should also be carefully considered.”⁵

The second major approach to substaging has used quantitation of the depth or volume of the invasive carcinoma. The literature here is less robust than for utilising MM. A review of several studies^{4,6-11} demonstrates that this approach also has merit. In two of these studies the authors measure the maximum depth of invasion perpendicular to the mucosal surface.^{6,11} This method has the difficulty of orientation of the fragments and identification of the mucosal surface or basement membrane. In other studies the measurement is based on the maximum linear length of the invasive tumour, irrespective of the orientation.^{4,7-11} Cut points have been 0.5 mm or 1.0 mm. The largest series (509 patients) that also had the longest follow up (median 81 months) utilized the 1.0 mm cut point (based on the sum of the maximum dimension of all invasive foci) and showed a strong correlation with recurrence free-, progression free- and cancer specific-survival.⁸

Recent guidelines have generally recommended that pathologists provide some indication of volume or depth of invasion without specifying a preferred method.¹² In the International Consultation on Urologic Disease (ICUD) recommendations for quantitation, Amin et al stated “It is recommended that pathologists provide some form of estimate of the lamina propria invasion in pT1 tumours (e.g. focal, multifocal, extensive, etc)” and “Involvement of the MM may be included in a comment to provide information on the depth/extent of invasion.” The 2016 WHO follows this recommendation as do the recently released College of American Pathologists reporting guidelines.^{12,13}

Clinical guidelines have also noted the importance of depth of invasion. In the ICUD section on treatment of high grade Ta, carcinoma in situ (CIS) and T1 urothelial carcinoma, the author’s first recommendation is “The assessment of T1 urothelial carcinoma should be based on tumour grade, early recurrence, multiplicity, tumour size, concomitant CIS, urothelial carcinoma involving the prostatic mucosa or ducts, and depth of invasion.”¹⁴

Because of the potential for additional information in T1 tumours to directly impact clinical decision making the International Collaboration on Cancer Reporting (ICCR) guidelines have included substaging of T1 disease as a non-required element. The dataset also provides for alternative methods for reporting as there is insufficient data to recommend one alternative over the others.

References

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