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TNM staging UICC

A commentary on imaging and the 8th edition of the UICC-TNM T category in prostate cancer.

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What's in a name? All the world is a stage

The first requirements of clinical management of prostate cancer are to classify patients into prognostic groups and to aid in decision-making on treatment options. Of all prognostic factors which determine outcome after prostate cancer treatment, the anatomical extent of disease is one of the most important – but certainly not the only factor. “Stage”, in truth, means *nothing more than the anatomical extent of disease*. Unification of clinical staging allows comparison of populations and is therefore crucial in public health and epidemiology as well as in the design of clinical trials, and routine clinical practice. Careful description of the tumor characteristics, on which to build a staging system, is mandatory. The TNM-staging is currently considered the cornerstone of tumor classification and is regularly updated as novel information provides sufficient evidence to underpin a change. Despite its many inconsistencies, TNM as a concept is a pragmatic, though imperfect system that has stood the test of time.

To improve outcome prediction, and for clinical management, stage has to be combined with other prognostic factors – notably PSA level and Gleason score or ISUP grade – to produce a prognostic risk stratification which will ultimately determine treatment. A common misconception is that stage (and TNM categories) are the same as a prognostic classification. They are not – rather, TNM categories (i.e the anatomical extent of disease) merely represent a major *component* of prognostic classification. This is acknowledged by both the UICC and AJCC versions of the TNM classification for prostate cancer. To combine stage with non-anatomical prognostic factors, something further is needed - the UICC defines only a stage group, and notes the major non-anatomical factors

such as PSA and grade, while the AJCC version has what they term a “prognostic stage group” classification, which (like the d’Amico risk classification) overtly incorporates factors other than extent of disease. The EAU Guidelines recommend following the UICC version of the classification, and it is important for public health and epidemiology not to confuse “stage” and “prognostic stage group”.

Imaging for extent of primary disease

Across the world, and across all cancer sites, there is variation in the way in which imaging is performed to assess tumour extent. In the case of lung cancer, for example, information from cross-sectional imaging can be used to help define a clinical T or N category. In the case of prostate cancer, prostate imaging was often incorporated in the clinical T category, but this introduces many inconsistencies. Firstly, there are great variations in the availability, quality, and expertise brought to bear on prostate imaging (for example with multiparametric MRI). Secondly, while modern imaging will identify patients who, for example, have subtle and early evidence of extraprostatic extension, these patients are manifestly different to patients with gross evidence of extraprostatic extension that is palpable by DRE. Simply calling them both “cT3” is an example of stage migration, and will mean that the radiologically staged patients have a far better prognosis and (arguably) might be over-treated compared with those whose locally advanced disease is clinically palpable. This is why, for the 8th edition of TNM, imaging is no longer used for the definition of T-category of prostate cancers¹.

What you record, and what you use, need not be the same as what you report to the cancer registry

The new EAU Prostate cancer-guidelines for 2019 now recommend mpMRI early in the diagnosis of prostate cancer, even before doing the first biopsy. Early diagnosis and possibly accurate delineation of the intraprostatic extent of prostate cancer can be improved by mpMRI^{2,3}. Should mpMRI findings be incorporated into future editions of TNM? Perhaps the time will come when advanced imaging is widely available, and when the precise delineation of intraprostatic disease volume makes a crucial difference to local treatment worldwide, but for organ-confined disease at least, it is unlikely to impact in a major way on overall survival, when other factors such as PSA and ISUP grade are accounted for. The sensitivity of mpMRI to identify microscopic extracapsular growth is low but mpMRI is superior in predicting established extracapsular growth on histology compared to nomograms and clinical staging⁴. Current nomograms include clinical T-stage mainly based on DRE⁵⁻⁷ and therefore incorrect prediction may be obtained when MRI is included in T-staging. Nomogram histological outcome prediction, however, can be improved by separately adding mpMRI data⁸. A radiologic-risk signature based on mpMRI was a better predictor of biochemical recurrence after prostatectomy when compared to the classic Kattan nomogram⁹ and using mpMRI instead of DRE for clinical staging improved the prediction of nodal metastases¹⁰. Therefore, recording the extent of disease in the prostate assessed on mpMRI, is perfectly justifiable, but if used should be added in a descriptive format rather than assigning and reporting a T-category based on it. It is important to distinguish

between what is *reported*, for example if UICC TNM stage is used for public health surveillance, and what is *used*, for example in daily practice. The exclusion of imaging from cT categorisation in no way means that imaging should not be done, or that the information should not be used for clinical decision making. It should be remembered that UICC TNM is intended to be used worldwide; however, sophisticated imaging such as mpMRI is most certainly not yet available worldwide.

An additional argument for routine prostate imaging in clinical practice is that with DRE, only the dorsal side of the prostate can be reliably palpated. Therefore, inclusion of imaging information from mpMRI alongside T-categorisation has the potential to improve accuracy of clinical assessment, especially where there is an anterior tumour. Again, though, such findings from imaging modalities should be used but reported as a description of the observations, rather than using them to assign and report a T-category.

Conclusions

The EAU Prostate cancer guidelines give specific recommendations about when to use imaging, and what sort of imaging to use. We must neither expect TNM to be a one-stop repository for all staging information nor should we imply that patients should only have those assessments done which feature in the TNM classification.

Confusion undoubtedly exists regarding the use of imaging data in defining and recording T-category. This article is written to draw attention to

this and to stress the importance of a uniform approach to T-category assignment. Image the prostate with modern MRI by all means, and use the results in clinical management, but *only the DRE result should be recorded for assigning a TNM clinical stage.*

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