COMMENTARY

The Process for Continuous Improvement of the TNM Classification

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The TNM classification is a worldwide benchmark for reporting the extent of malignant disease and is a major prognostic factor in predicting the outcome of patients with cancer. The objectives for cancer staging were defined by the International Union Against Cancer (UICC) TNM Committee almost 50 years ago and are still broadly applicable today. To keep pace with the modern demands of evidence-based practice, the UICC introduced a structured process for introducing changes to the TNM classification. The elements of the TNM process were determined to include the development of unambiguous criteria for the information and documentation required to consider changes in the classification, establishment of a well-defined process for the annual review of relevant literature, formation of site-specific expert panels, and the participation of experts from all over the world in the TNM review process. Communication between the oncology community and those involved in the TNM classification was established as being essential to the success of the process. The process, which was introduced in 2002, will be tested over the next 3–4 years and evaluated. In addition to the formal process, individual initiative, involvement by the national staging committees, and group consensus are required. Furthermore, increased involvement by the experts should improve the understanding and dissemination of the TNM classification. ***Cancer* 2004;100:1–5.**
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Cancer staging is one of the fundamental activities in oncology. The knowledge of the extent of disease is required to characterize the disease before selecting treatment. The key pieces of information needed for the management and reporting of results in patients with cancer are presenting site, histologic type, and the anatomic extent of disease. Malignancies are classified according to the International Classification of Diseases for Oncology coding system for the presenting site and the histologic type, where World Health Organization classification of tumors is also available. Assessment of the anatomic extent of disease extent at diagnosis is classified using staging classification. The TNM system for classifying the anatomic extent of disease in cancer has been in existence for more than 50 years. With time and sequential editions, the TNM classification has evolved to accommodate new knowledge. The current (sixth) edition was published in 2002.[1,2] The TNM classification is used worldwide and is a benchmark for reporting the extent of disease and is a major prognostic factor in predicting the outcome of patients with cancer. The objectives for cancer staging were defined by the International Union Against Cancer (UICC) TNM Committee almost 50 years ago (Table 1).[3,4]

TABLE 1
Objectives of the TNM Classification

To aid the clinician in planning treatment
To give some indication of prognosis
To assist in evaluating the results of treatment
To facilitate the exchange of information between treatment centers
To contribute to continuing investigations of human malignancies

The TNM classification system is applied in a variety of situations.[5,6] For example, cancer registries and health services researchers want a stable classification for the purpose of comparing data and accessing outcomes over long periods of time. In contrast, clinicians prefer a more adaptable classification that is relevant to contemporary clinical practice, that reflects clinical advancements, and that is helpful in identifying appropriate treatment options. Overall, the system is immeasurably useful and is a foundation of clinical decision-making and clinical practice guidelines.[6] It is widely accepted that the anatomic extent of disease is not the sole factor that needs to be considered in reaching treatment decisions and predicting the outcome.[7] There are numerous nonanatomic prognostic factors that affect the course of disease, response to treatment, and the ultimate prognosis.[8] These are not considered in the current study, and the process for their adoption and modification should be addressed in a separate study.

The TNM classification system has been modified over the years, mainly to improve its prognostic ability and to keep pace with the demands of clinical practice.[9] Historically, changes to the TNM classification were derived from a decision-making process based on expert opinion from several national TNM committees and from the individual membership of the UICC TNM Committee. However, complex changes have emerged that have made it increasingly difficult to use the previous procedures to review and assess proposals for changes and to make appropriate, evidence-based decisions. There has been explosive growth in medical research, knowledge, and information. Proposals for changes to the TNM classification vary widely in their format and content and frequently provide insufficient information for properly assessing the value or validity of the proposed changes. Proposals often lack consistency in the amount and quality of supporting data submitted. No formal or systematic process was used routinely for gathering the opinions of a diverse body of experts outside the TNM Committee structure or for identifying opportunities for changes from the literature. There was inconsistency in the statistical rigor (e.g., there was an insufficient number of patients/cases in studies, leading to questions of statistical power, reliability, and scientific validity; in addition, the statistical methods used were not described in the proposal) and in the decision criteria applied to the proposals for TNM changes. There was no existing method for evaluating the strength or quality of the data in support of changes to the TNM classification, nor was there a routine way to relay the decisions of the UICC TNM Committee to the authors who proposed the recommended changes.

The process of developing and reviewing proposals and making changes to the TNM classification must evolve to continue to meet the needs of those who use the TNM classification. The UICC TNM Committee recently reviewed its operations and developed a process for continuous improvement of the TNM classification. The new process expands the methods and tools for evaluating proposed changes to the TNM system and emphasizes the continuous monitoring, improvement, and adaptation of the TNM. Therefore, the quality of the evidence provided is the main focus of the new process. The UICC Committee recognizes that this process requires a multidisciplinary approach and the inclusion of all involved in the treatment of patients with cancer and in the reporting of outcome data.

In developing a process for continuous review, we identified two key activities. The first is the process for considering the proposals to revise the TNM or to create a new classification. The second is the contin-

TABLE 2
Proposals for Revisions to the TNM Classification: Information Required

Name of the proposing individual, group, or country
Tumor site and tumor morphology (including ICD-O-3 codes)
Rationale for suggesting the change and the clinical context surrounding the rationale
Years of diagnosis of the patient cohort under consideration in the proposal
Description of the cohort (i.e., age profile, gender profile, race/ethnicity profile if relevant).
Description of the referral pattern of patients from the communities to the institution(s) represented in the proposal's cohort (e.g., is the institution mostly tertiary care?)
Description of the selection process for the population under study (e.g., inception cohort, convenience sample, random sample etc)
The TNM classification (i.e., edition and version) used in the proposal's analysis.
Description of additional essential prognostic factors relevant to the proposal
Description of profile of therapeutic interventions received by the cohort in the proposal (e.g., surgery, radiation, chemotherapy, adjuvant therapy, neoadjuvant therapy)
Description of endpoints used in the proposal (e.g., mortality, disease recurrence)
Analyses addressing the stated goal(s) of the study
Analyses contrasting the predictive ability of the current TNM system with that of the proposed system
Analyses including inferential statistical comparisons of the current system and the proposed system
Description and/or citation of unconventional statistical methods
Specific recommendations for revision of the TNM classification
Results and interpretation of statistical analyses
Limitations of the data presented in the proposal
Relation of the proposal to published literature and current practice patterns

ICD-O: International Classification of Diseases for Oncology.

uous literature review that identifies opportunities for improving the system. The process for continuous improvement of the TNM as described in the current study is being tested (i.e., from 2002 to 2005) to further refine the criteria.

MATERIALS AND METHODS

The International Union Against Cancer TNM Classification Review Process

To coordinate the implementation of changes to the TNM classification, we have established a new method for receiving, processing, and coordinating a review of the proposals for change. Proposals for changes to the classification can be received from any constituency. They can be submitted directly to the TNM Committee from its members, from national TNM committees, from specialty organizations, or from other stakeholders. The proposals for revision of the TNM classification should contain a basic amount of required information that would help the committee to assess the specific goal of the proposal and the information on which the proposal is based. The requirements for the proposals are outlined in Table 2. Upon receipt of the proposal to amend or change the classification, the TNM Process Subcommittee will assess the completeness of the proposal and the use of the appropriate statistical methods, review the availability of internal and external validation, and evaluate the clinical context of the proposed change. Incomplete proposals will be returned to the authors.

TABLE 3
Criteria for Instituting Changes to the TNM Classification

Clinical relevance in terms of assessment, treatment, and outcome
Presence of evidence for improved prognostic ability
Acceptance by the members of UICC TNM Committee

UICC: International Union Against Cancer.

The process of reviewing complete proposals will include the review and opinions from newly established UICC TNM Expert Panels (see section later in the text). To ensure uniform TNM classification criteria, the Expert Panel membership will reflect a joint collaboration between the American Joint Committee on Cancer (AJCC) and the UICC TNM Committee. The involvement of both groups will aid in making the TNM classification more uniform. The information and the opinions of the Expert Panel will be summarized, and a report will be generated. Recommendations from the TNM Process Subcommittee will be forwarded to the entire TNM Committee for a review and decision. Table 3 shows the criteria for instituting changes to the TNM.

The disposition of each proposal will be communicated to the authors and the decisions of the committee will be specified. In addition to the publication of the original findings by the proposal originators, it is expected that all new proposals for changes approved by the TNM Committee will be published in peer-reviewed literature. The publication should be a collaboration between the entire TNM Committee and the authors of the proposal. An expert on staging will be selected by the TNM Committee to represent the input of its members. The preferred method of publication will be the major oncology-related journals. The proposals also will be communicated on the UICC TNM website (URL: http://www.uicc.org/programmes/detection/tnm/tnmfaqs.shtml).

RESULTS

Continuous Literature Review—TNM Classification

The past experience of the TNM Committee is that the proposals for change in the classification may not be forthcoming even for disease sites where the classification is poorly accepted, poorly used, or continuously criticized in the literature. To identify new op-

TABLE 4
Annual Literature Review

Goals
To identify new opportunities to improve the TNM classification
To review criticism of the existing TNM classification
To identify gaps in the TNM classification, specifically in areas where no classification exists
To review proposals for amendments to the TNM system that should be evaluated by the TNM prognostic factors committee
To review proposals for new classifications by the TNM prognostic factors committee
To gather evidence for the use of the TNM classification in clinical research and outcome research
Search strategy
Neoplasm staging—major MESH
TNM (in title/abstract) and neoplasm staging (minor MESH)
UICC (in title/abstract) and neoplasm staging (minor MESH)
AJCC (in title/abstract) and neoplasm staging (minor MESH)
FIGO (in title/abstract) and neoplasm staging (minor MESH)

UICC: International Union Against Cancer; MESH: medical subject headings; AJCC: American Joint Committee on Cancer; FIGO: International Federation of Gynecology and Obstetrics.

portunities for improvement, review the criticisms, and identify gaps in the TNM classification, the TNM Process Subcommittee has developed, piloted, and tested a mechanism for continuous review, referred to as the 'literature watch' (Table 4).

The TNM Process Subcommittee has embarked on an annual literature review using a predetermined search strategy (Table 4) and a subsequent triaging of the material identified in the published literature. The triaged literature is sorted into major disease site groupings (e.g., breast carcinoma, head and neck carcinoma, genitourinary carcinomas) and reviewed. The sorted literature then is distributed to the TNM Committee and to the members of the UICC TNM Expert Panels. The UICC TNM Expert Panels are to determine whether the published literature indicates a need for the revision of the classification. The TNM Process Subcommittee then evaluates the input from the experts and others, synthesizes the information, and presents the final recommendation to the entire TNM Committee at its annual meeting each May. The literature watch does not address the issues of the use, or the accuracy, of a particular staging test or method, but is focused only on classifying the anatomic extent of disease. It excludes the literature dealing with nonanatomic prognostic factor classification. The timing of the annual literature watch is coordinated with the annual meeting of the TNM Committee.

DISCUSSION

International Union Against Cancer TNM Expert Panels

With limited membership, the UICC TNM Committee does not encompass the wide spectrum of expertise required to render opinion on all areas of cancer staging and is unable to represent the interests of all disciplines that use the TNM classification. To obtain the input of a broader group of experts dealing with cancer in their practice and in their research activities, the UICC has invited a multidisciplinary cadre of experts in major disease sites to assist them in judging the current status, or any new development, in the cancer staging classification. The goal of this initiative is to provide added credibility to the TNM review and improvement process. Membership in the UICC TNM Expert Panels is multidisciplinary and consists of surgeons, radiation oncologists, medical oncologists, pathologists, epidemiologists, and statisticians. As much as possible, membership represents diverse geographic regions of the world. The members are widely recognized for their expertise in a given area of cancer. In addition, the UICC TNM Expert Panels include members of national committees on cancer staging. Specifically, there is strong representation by members of the AJCC Task Forces and the International Federation of Gynecology and Obstetrics. Selection is based on interest in staging issues, publication record, and a willingness to serve. The members are named as consultants to the TNM Committee and accept a mandate to serve on site-specific panels for a minimum term of 3 years.

To conclude, the knowledge and practice of medicine and oncology are constantly undergoing change. Our ability to diagnose cancer early, to characterize tumors, to assess disease extent, and to treat improves each year. The TNM system for classification of the anatomic disease extent has served oncology well for $>$ 50 years. However, it needs to keep pace with progress. Changes to the TNM classification have been based on individual initiatives and a consensus developed by members of the national TNM committees and task forces. We have now introduced a more structured process for introducing changes to the TNM classification that is increasingly evidence based. The process was introduced in 2002 and will be tested over the next 3–4 years and evaluated. This process will not diminish the need for individual initiative, involvement by the national staging committees, and group consensus, but will enhance it. Increased involvement by the experts in each field should also improve the understanding and dissemination of the TNM classification.

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