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They are called wise
who put things in their right order

Thomas Aquinas

This Eighth Edition is dedicated to Dr Leslie H. Sobin MD, a pathologist and previous long term Chair of UICC TNM Prognostic Factor Committee. Les, as he is known to colleagues all over the world, has devoted most of his career to help promote globally unified classifications of disease in particular in pathology and cancer staging. This is the first edition since the fourth that has not benefitted from his direct involvement; however his imprint is found throughout this edition.
Preface

In this eighth edition of *TNM Classification of Malignant Tumours*, many of the tumour sites are unchanged from the seventh edition. However, some tumour entities and anatomic sites have been newly introduced and some tumours contain modifications: this follows the basic philosophy of maintaining stability of the classification over time. The modifications and additions reflect new data on prognosis as well as new methods for assessing prognosis. Some changes had already appeared in the *TNM Supplement* as proposals. Subsequent support warrants their incorporation into the classification. New proposals for tumours of parathyroid carcinoma, and paraganglioma will be published in the next edition of the *TNM Supplement*.

In the seventh edition a new approach was adopted to separate stage groupings from prognostic groupings in which other prognostic factors are added to T, N, and M categories. These new prognostic groupings were presented for oesophagus and prostate. In this eighth edition, the term ‘stage’ is used when only descriptions of anatomic extent of disease are used and ‘prognostic group’ for when additional prognostic factors are incorporated.

Changes made between the seventh and eighth editions are indicated by a bar at the left hand side of the text. To avoid ambiguity, users are encouraged to cite the edition and year of the TNM publication they have used in their list of references.

A TNM homepage with Frequently Asked Questions (FAQs) and a form for submitting questions or comments on the TNM can be found at: [http://www.uicc.org](http://www.uicc.org).

The UICC’s TNM Prognostic Factors Project has a process for evaluating proposals to change the TNM Classification. This procedure aims at a continuous systematic approach composed of two arms: (1) review formal proposals from investigators and (2) an annual literature search for articles concerning improvements to TNM. The proposals and results of the literature search are evaluated by a UICC panel of experts as well as by the TNM Prognostic Factors committee members. The national TNM Committees participated in this process. More details and a checklist that will facilitate the formulation of proposals can be obtained at [www.uicc.org](http://www.uicc.org).

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References


Acknowledgments

The Editors have much pleasure in acknowledging the great help received from the members of the TNM Prognostic Factors Project Committee and the National Staging Committees Global Representatives and international organizations listed on pages xvi, all of whom volunteered their time.

We thank Professor Patti Groome and Ms Colleen Webber for supervising and performing the literature watch from its inception until 2015 and 2016, respectively. The eighth edition of the *TNM Classification* is the result of a number of consultative meetings organized and supported by the UICC and AJCC secretariats.

This publication was made possible by grants 1U58DP001818 and 1U58DP004965 from the Centers for Disease Control and Prevention (CDC) (USA). Its contents are solely the responsibility of the authors and do not necessarily represent the official views of the CDC.
Organizations Associated with the TNM System

- CDC  Centers for Disease Control and Prevention (USA)
- FIGO  International Federation of Gynaecology and Obstetrics
- IACR  International Association of Cancer Registries
- IARC  International Agency for Research on Cancer
- IASLC  International Association for the Study of Lung Cancer
- ICCR  International Collaboration on Cancer Reporting
- WHO  World Health Organization

National Committees

- Australia and New Zealand  National TNM Committee
- Austria, Germany, Switzerland  Deutschsprachiges TNM-Komitee
- Belgium  National TNM Committee
- Brazil  National TNM Committee
- Canada  National Staging Steering Committee
- China  National TNM Cancer Staging Committee of China
- Denmark  National TNM Committee
- Gulf States  TNM Committee
- India  National TNM Committee
- Israel  National Cancer Staging Committee
- Italy  Italian Prognostic Systems Project
- Japan  Japanese Joint Committee
- Latin America and the Caribbean  Sociedad Latinoamericana y del Caribe de Oncología Médica
- Netherlands  National Staging Committee
- Poland  National Staging Committee
- Singapore  National Staging Committee
- Spain  National Staging Committee
- South Africa  National Staging Committee
- Turkey  Turkish National Cancer Staging Committee
- United Kingdom  National Staging Committee
- United States of America  American Joint Committee on Cancer
Members of UICC Committees Associated with the TNM System

In 1950 the UICC appointed a Committee on Tumour Nomenclature and Statistics. In 1954 this Committee became known as the Committee on Clinical Stage Classification and Applied Statistics and in 1966 it was named the Committee on TNM Classification. Taking into consideration new prognostic factors the Committee was named in 1994 the TNM Prognostic Factors Project Committee, and in 2003 the main committee was named “TNM Prognostic Factors Core Group”. A list of members who have served on these committees is available at: www.uicc.org

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In addition, the Editors wish to acknowledge the invaluable contributions of:

**Head and Neck Cancers**  
UICC Advisory Committee (see [www.uicc.org](http://www.uicc.org))

**Thymic Tumours**  
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See [www.uicc.org](http://www.uicc.org)
Introduction

The History of the TNM System*

The TNM system for the classification of malignant tumours was developed by Pierre Denoix (France) between the years 1943 and 1952.¹

In 1950, the UICC appointed a Committee on Tumour Nomenclature and Statistics. As a basis for its work on clinical stage classification, it adopted the general definitions of local extension of malignant tumours suggested by the World Health Organization (WHO) Sub.Committee on The Registration of Cases of Cancer as well as Their Statistical Presentation.²

In 1958, the Committee published the first recommendations for the clinical stage classification of cancers of the breast and larynx and for the presentation of results.³

A second publication in 1959 presented revised proposals for the breast, for clinical use and evaluation over a 5 year period (1960–1964).⁴ In 1968, a booklet, the Livre de Poche⁵ and, a year later, a complementary booklet was published detailing recommendations for the setting up of field trials, for the presentation of end results, and for the determination and expression of cancer survival rates.⁶ The Livre de Poche was subsequently translated into 11 languages. In 1974 and 1978, second and third editions⁷,⁸ were published containing new site classifications, and the fourth edition of TNM in 1987.⁹

In 1993, the project published the TNM Supplement¹⁰ to promote the uniform use of TNM by providing detailed explanations of the TNM rules with practical examples. Second, third, and fourth editions appeared in 2001, 2003, and 2012.¹¹–¹³

The project also publishes the TNM Atlas an Illustrated Guide to the TNM Classification of Malignant Tumours, the sixth edition was published in 2014 as a companion to the seventh edition of the TNM Classification.¹⁴

In 1995, the project published Prognostic Factors in Cancer,¹⁵ a compilation and discussion of prognostic factors in cancer, both anatomical and non-anatomical, at each of the body sites. This was expanded in the second edition in 2001¹⁶ and the third edition in 2006.¹⁷

The current eighth edition of TNM contains rules of classification and staging that correspond with those appearing in the eighth edition of the AJCC Cancer Staging Manual (2017).¹⁸ While the aim of the UICC and AJCC is to have identical classifications, small differences exist and are identified as footnotes to the text. Wherever possible, the UICC classification is based on published evidence based recommendation.

To develop and sustain a classification system acceptable to all requires the closest liaison
between national and international organizations. As noted, while the classification is based on published evidence, in areas where high-level evidence is not available it is based on international consensus. The continuing objective of the UICC is to present the classification of anatomical extent of cancer globally.

**Note**

* A more detailed history is available on the website at [www.uicc.org](http://www.uicc.org)

**The Principles of the TNM System**

The practice of classifying cancer cases into groups according to anatomical extent, termed ‘stage’, arose from the observation that survival rates were higher for cases in which the disease was localized than for those in which the disease had extended beyond the organ of origin. The stage of disease at the time of diagnosis is a reflection not only of the rate of growth and extension of the neoplasm but also the type of tumour and the tumour–host relationship.

It is important to record accurate information on the anatomical extent of the disease for each site at the time of diagnosis, to meet the following objectives:

1. to aid the clinician in the planning of treatment
2. to give some indication of prognosis for survival
3. to assist in evaluation of the results of treatment
4. to facilitate the exchange of information between treatment centres
5. to contribute to the continuing investigation of human cancer
6. to support cancer control activities.

Cancer staging is essential to patient care, research, and cancer control. Cancer control activities include direct patient care related activities, the development and implementation of clinical practice guidelines, and centralized activities such as recording disease extent in cancer registries for surveillance purposes and planning cancer systems. Recording of stage is essential for the evaluation of outcomes of clinical practice and cancer programmes. However, in order to evaluate the long-term outcomes of populations, it is important for the classification to remain stable. There is therefore a conflict between a classification that is updated to include the most current forms of medical knowledge while also maintaining a classification that facilitating longitudinal studies. The UICC TNM Project aims to address both needs.

International agreement on the classification of cancer by extent of disease provides a method of conveying disease extent to others without ambiguity.

There are many axes of tumour classification: for example, the anatomical site and the clinical and pathological extent of disease, the duration of symptoms or signs, the gender and age of the patient, and the histological type and grade of the tumour. All of these have
an influence on the outcome of the disease. Classification by anatomical extent of disease is the one with which the TNM system primarily deals.

The clinician's immediate task when meeting a patient with a new diagnosis of cancer is to make a judgment as to prognosis and a decision as to the most effective course of treatment. This judgment and this decision require, among other things, an objective assessment of the anatomical extent of the disease.

To meet the stated objectives a system of classification is needed:

1. that is applicable to all sites regardless of treatment; and
2. that may be supplemented later by further information that becomes available from histopathology and/or surgery.

The TNM system meets these requirements.

The General Rules of the TNM System

The TNM system for describing the anatomical extent of disease is based on the assessment of three components:

- T – the extent of the primary tumour
- N – the absence or presence and extent of regional lymph node metastasis
- M – the absence or presence of distant metastasis.

The addition of numbers to these three components indicates the extent of the malignant disease, thus:

\[ T0, T1, T2, T3, T4, N0, N1, N2, N3, M0, M1 \]

In effect, the system is a ‘shorthand notation’ for describing the extent of a particular malignant tumour.

The general rules applicable to all sites are as follows:

1. All cases should be confirmed microscopically. Any cases not so proved must be reported separately.
2. Two classifications are described for each site, namely:
   a. **Clinical classification**: the pretreatment clinical classification designated **TNM** (or cTNM) is essential to select and evaluate therapy. This is based on evidence acquired before treatment. Such evidence is gathered from physical examination, imaging, endoscopy, biopsy, surgical exploration, and other relevant examinations.
   b. **Pathological classification**: the postsurgical histopathological classification, designated **pTNM**, is used to guide adjuvant therapy and provides additional data to estimate prognosis and end results. This is based on evidence acquired before treatment, supplemented or modified by additional evidence acquired from surgery and from pathological examination. The pathological assessment of the primary
tumour (pT) entails a resection of the primary tumour or biopsy adequate to evaluate the highest pT category. The pathological assessment of the regional lymph nodes (pN) entails removal of the lymph nodes adequate to validate the absence of regional lymph node metastasis (pN0) or sufficient to evaluate the highest pN category. An excisional biopsy of a lymph node without pathological assessment of the primary is insufficient to fully evaluate the pN category and is a clinical classification. The pathological assessment of distant metastasis (pM) entails microscopic examination of metastatic deposit.

3. After assigning T, N, and M and/or pT, pN, and pM categories, these may be grouped into stages. The TNM classification and stages, are established at diagnosis and must remain unchanged in the medical records.

Only for cancer surveillance purposes, clinical and pathological data may be combined when only partial information is available either in the pathological classification or the clinical classification.

4. If there is doubt concerning the correct T, N, or M category to which a particular case should be allotted, then the lower (i.e., less advanced) category should be chosen. This will also be reflected in the stage.

5. In the case of multiple primary tumours in one organ, the tumour with the highest T category should be classified and the multiplicity or the number of tumours should be indicated in parenthesis, e.g., T2(m) or T2(5). In simultaneous bilateral primary cancers of paired organs, each tumour should be classified independently. In tumours of the liver, ovary and fallopian tube, multiplicity is a criterion of T classification, and in tumours of the lung multiplicity may be a criterion of the M classification.

6. Definitions of the TNM categories and stage may be telescoped or expanded for clinical or research purposes as long as the basic definitions recommended are not changed. For instance, any T, N, or M can be divided into subgroups.

Notes

a For more details on classification the reader is referred to the TNM Supplement.

b An educational module is available on the UICC website www.uicc.org.

Anatomical Regions and Sites

The sites in this classification are listed by code number of the International Classification of Diseases for Oncology. Each region or site is described under the following headings:

- Rules for classification with the procedures for assessing the T, N, and M categories
- Anatomical sites, and subsites if appropriate
- Definition of the regional lymph nodes
TNM Clinical Classification

The following general definitions are used throughout:

T – Primary Tumour

TX  Primary tumour cannot be assessed
To  No evidence of primary tumour
Tis  Carcinoma in situ
T1–T4 Increasing size and/or local extent of the primary tumour

N – Regional Lymph Nodes

NX  Regional lymph nodes cannot be assessed
N0  No regional lymph node metastasis
N1–N3 Increasing involvement of regional lymph nodes

M – Distant Metastasis *

M0  No distant metastasis
M1  Distant metastasis

Note

* The MX category is considered to be inappropriate as clinical assessment of metastasis can be based on physical examination alone. (The use of MX may result in exclusion from staging.)

The category M1 may be further specified according to the following notation:

- Pulmonary    PUL (C34)
- Osseous      OSS (C40, 41)
- Hepatic      HEP (C22)
- Brain        BRA (C71)
- Lymph nodes  LYM (C77)
Subdivisions of some main categories are available for those who need greater specificity (e.g., T1a, T1b or N2a, N2b).

**pTNM Pathological Classification**

The following general definitions are used throughout:

**pT – Primary Tumour**
- pTX: Primary tumour cannot be assessed histologically
- pTo: No histological evidence of primary tumour
- pTis: Carcinoma in situ
- pT1–4: Increasing size and/or local extent of the primary tumour histologically

**pN – Regional Lymph Nodes**
- pNX: Regional lymph nodes cannot be assessed histologically
- pN0: No regional lymph node metastasis histologically
- pN1–3: Increasing involvement of regional lymph nodes histologically

**Notes**
- Direct extension of the primary tumour into lymph nodes is classified as lymph node metastasis.
- Tumour deposits (satellites), i.e., macro. or microscopic nests or nodules, in the lymph drainage area of a primary carcinoma without histological evidence of residual lymph node in the nodule, may represent discontinuous spread, venous invasion (V1/2) or a totally replaced lymph node. If a nodule is considered by the pathologist to be a totally replaced lymph node (generally having a smooth contour), it should be recorded as a positive lymph node, and each such nodule should be counted separately as a lymph node in the final pN determination.
- Metastasis in any lymph node other than regional is classified as a distant metastasis.
- When size is a criterion for pN classification, measurement is made of the metastasis,
not of the entire lymph node. The measurement should be that of the largest
dimension of the tumour.

- Cases with micrometastasis only, i.e., no metastasis larger than 0.2 cm, can be
identified by the addition of ‘(mi)’, e.g., pN1(mi).

### Sentinel Lymph Node

The sentinel lymph node is the first lymph node to receive lymphatic drainage from a
primary tumour. If it contains metastatic tumour this indicates that other lymph nodes
may contain tumour. If it does not contain metastatic tumour, other lymph nodes are not
likely to contain tumour. Occasionally, there is more than one sentinel lymph node.
The following designations are applicable when sentinel lymph node assessment is
attempted:

- (p)NX(sn) Sentinel lymph node could not be assessed
- (p)N0(sn) No sentinel lymph node metastasis
- (p)N1(sn) Sentinel lymph node metastasis

### Isolated Tumour Cells

Isolated tumour cells (ITC) are single tumour cells or small clusters of cells not more
than 0.2 mm in greatest extent that can be detected by routine H and E stains or
immunohistochemistry. An additional criterion has been proposed in breast cancer to
include a cluster of fewer than 200 cells in a single histological cross-section. Others have
proposed for other tumour sites that a cluster should have 20 cells or fewer; definitions of
ITC may vary by tumour site. ITCs do not typically show evidence of metastatic activity
(e.g., proliferation or stromal reaction) or penetration of vascular or lymphatic sinus
cells. Cases with ITC in lymph nodes or at distant sites should be classified as No or Mo,
respectively. The same applies to cases with findings suggestive of tumour cells or their
components by non-morphological techniques such as flow cytometry or DNA analysis.
The exceptions are in malignant melanoma of the skin and Merkel cell carcinoma,
wherein ITC in a lymph node are classified as N1. These cases should be analysed
separately. Their classification is as follows.

- (p)No No regional lymph node metastasis histologically, no examination for
  isolated tumour cells (ITC)
- (p)No(i−) No regional lymph node metastasis histologically, negative morphological
  findings for ITC
- (p)No(i+) No regional lymph node metastasis histologically, positive morphological
  findings for ITC
- (p)No(mol−) No regional lymph node metastasis histologically, negative non-
  morphological findings for ITC
(p)No(mol+)  No regional lymph node metastasis histologically, positive non-morphological findings for ITC

Cases with or examined for isolated tumour cells (ITC) in sentinel lymph nodes can be classified as follows:

(p)No(i−)  No sentinel lymph node metastasis histologically, negative morphological findings for ITC

(p)No(i+)  No sentinel lymph node metastasis histologically, positive morphological findings for ITC

(p)No(mol−)  No sentinel lymph node metastasis histologically, negative non-morphological findings for ITC

(p)No(mol+)  No sentinel lymph node metastasis histologically, positive non-morphological findings for ITC

\textbf{pM – Distant Metastasis} *

\textit{pM1} Distant metastasis microscopically confirmed

\textbf{Note}

* pM0 and pMX are not valid categories.

The category pM1 may be further specified in the same way as M1 (see page 6).

\textbf{Isolated tumour cells} found in bone marrow with morphological techniques are classified according to the scheme for N, e.g., M0(i+). For non-morphological findings ‘mol’ is used in addition to M0, e.g., M0 (mol+).

\textbf{Histopathological Grading}

In most sites, further information regarding the primary tumour may be recorded under the following heading:

\textbf{G – Histopathological Grading}

GX Grade of differentiation cannot be assessed
G1 Well differentiated
G2 Moderately differentiated
G3 Poorly differentiated
G4 Undifferentiated

\textbf{Notes}

- Grades 3 and 4 can be combined in some circumstances as ‘G3.4, poorly differentiated
Special systems of grading are recommended for tumours of breast, corpus uteri, and prostate.

**Additional Descriptors**

For identification of special cases in the TNM or pTNM classification, the m, y, r, and a symbols may be used. Although they do not affect the stage grouping, they indicate cases needing separate analysis.

**m Symbol.** The suffix m, in parentheses, is used to indicate the presence of multiple primary tumours at a single site. See TNM rule no. 5.

**y Symbol.** In those cases in which classification is performed during or following multimodality therapy, the cTNM or pTNM category is identified by a y prefix. The ycTNM or ypTNM categorizes the extent of tumour actually present at the time of that examination. The y categorization is not an estimate of the extent of tumour prior to multimodality therapy.

**r Symbol.** Recurrent tumours, when classified after a disease-free interval, are identified by the prefix r.

**a Symbol.** The prefix a indicates that classification is first determined at autopsy.

**Optional Descriptors**

**L – Lymphatic Invasion**

- LX Lymphatic invasion cannot be assessed
- L0 No lymphatic invasion
- L1 Lymphatic invasion

**V – Venous Invasion**

- VX Venous invasion cannot be assessed
- V0 No venous invasion
- V1 Microscopic venous invasion
- V2 Macroscopic venous invasion

**Note**

Macroscopic involvement of the wall of veins (with no tumour within the veins) is classified as V2.

**Pn – Perineural Invasion**
Residual Tumour (R) Classification*

The absence or presence of residual tumour after treatment is described by the symbol R. More details can be found in the TNM Supplement (see Preface, Reference 3).

TNM and pTNM describe the anatomical extent of cancer in general without considering treatment. They can be supplemented by the R classification, which deals with tumour status after treatment. It reflects the effects of therapy, influences further therapeutic procedures, and is a strong predictor of prognosis.

The definitions of the R categories are:

- RX  Presence of residual tumour cannot be assessed
- R0  No residual tumour
- R1  Microscopic residual tumour
- R2  Macroscopic residual tumour.

Note

* Some consider the R classification to apply only to the primary tumour and its local or regional extent. Others have applied it more broadly to include distant metastasis. The specific usage should be indicated when the R is used.

Stage and Prognostic Groups

The TNM system is used to describe and record the anatomical extent of disease. For purposes of tabulation and analysis it is useful to condense these categories into groups. For consistency, in the TNM system, carcinoma in situ is categorized stage 0; in general, tumours localized to the organ of origin as stages I and II, locally extensive spread, particularly to regional lymph nodes as stage III, and those with distant metastasis as stage IV. The stage adopted is such as to ensure, as far as possible, that each group is more or less homogeneous in respect of survival, and that the survival rates of these groups for each cancer site are distinctive.

For pathological stages, if sufficient tissue has been removed for pathological examination to evaluate the highest T and N categories, M1 may be either clinical (cM1) or pathological (pM1). However, if only a distant metastasis has had microscopic confirmation, the classification is pathological (pM1) and the stage is pathological.

Although the anatomical extent of disease, as categorized by TNM, is a very powerful prognostic indicator in cancer, it is recognized that many factors have a significant impact
on predicting outcomes. This has resulted in different stage groups. In thyroid cancer there are different stage definitions for different histologies and, new to this edition, in oropharyngeal cancer HPV related cancer is staged differently from non-HPV related cancer. Some factors have been combined with TNM in the development of stage groupings; for instance, for different histologies (thyroid), different major prognostic factor groups (age in thyroid), and by aetiology (HPV related oropharyngeal cancer). In this edition the term stage has been used as defining the anatomical extent of disease while prognostic group for classifications that incorporate other prognostic factors. Historically, age in differentiated thyroid cancer and grade in soft tissue sarcoma are combined with anatomical extent of disease to determine stage, and stage is retained rather than prognostic group in these two sites.

Prognostic Factors Classification

Prognostic factors can be classified as those pertaining to:

- **Anatomic extent of disease**: describes the extent of disease in the patient at the time of diagnosis. Classically, this is TNM but may also include tumour markers that reflect tumour burden, for instance prostate specific antigen (PSA) in prostate carcinoma or carcinoembryonic antigen (CEA) in colorectal carcinoma.

- **Tumour profile**: this includes pathological (i.e., grade) and molecular features of a tumour, and gene expression patterns that reflect behaviour. These can be:
  - predictive factors
  - prognostic factors
  - companion diagnostic marker.

- **Patient profile**: this includes terms related to the host of the cancer. These can be demographic factors, such as age and gender, or acquired, such as immunodeficiency and performance status.

- **Environment**: this may include treatment related and education (expertise, access, ageism, and healthcare delivery) and quality of management.

When describing prognostic factors it is important to state what outcome the factors are prognostic for, and at what point in the patient trajectory. Anatomical extent of disease as described by TNM stage defines prognosis for survival.

In the second edition of the *UICC TNM Classification of Malignant Tumours* for each tumour site, grids were developed that identified prognostic factors for survival at time of diagnosis and whether they were considered to be essential, additional, or new and promising. The grids were updated for the third edition and have been further updated and incorporated into the ninth edition of the *UICC Manual of Clinical Oncology*. Essential factors are those that are required in addition to anatomical extent of disease to determine treatment as identified by published clinical practice guidelines. The table is a generic example of the prognostic factors summary grid. The grids from the ninth edition
Examples of the UICC prognostic factors summary ‘grid’

<table>
<thead>
<tr>
<th>Prognostic factors</th>
<th>Tumour related</th>
<th>Host related</th>
<th>Environment related</th>
</tr>
</thead>
<tbody>
<tr>
<td>Essential*</td>
<td>Anatomical disease extent</td>
<td>Age</td>
<td>Availability of access to radiotherapy</td>
</tr>
<tr>
<td></td>
<td>Histological type</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Additional</td>
<td>Tumour bulk</td>
<td>Race</td>
<td>Expertise of a treatment at the specific level (e.g., surgery or radiotherapy)</td>
</tr>
<tr>
<td></td>
<td>Tumour marker level</td>
<td>Gender</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Programmed death 1 (PD.1) receptor and its ligands (PD. L1)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>New and promising</td>
<td>Epidermal growth factor receptor</td>
<td>Germline p53</td>
<td>Access to information</td>
</tr>
<tr>
<td></td>
<td>Gene expression patterns</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* The origin of essential factors as imperatives for treatment decisions are from known and available clinical practice guidelines.


**Essential TNM**

Information on anatomical extent of disease at presentation or stage is central to cancer surveillance to determine cancer burden as it provides additional valuable information to incidence and mortality data.\(^{22}\) However, cancer registries in low and middle income countries frequently have insufficient information to determine complete TNM data, either because of inability to perform necessary investigations or because of lack of recording of information. In view of this, the UICC TNM Project has with the International Agency for Research in Cancer and the National Cancer Institute developed a new classification system ‘Essential TNM’ that can be used to collect stage data when complete information is not available. To date, Essential TNM schemas have been developed for breast, cervix, colon, and prostate cancer, and are presented in this edition and available for download at [www.uicc.org](http://www.uicc.org).

**Paediatric Tumours**

Since the fourth edition, the UICC TNM Classification of Malignant Tumours has not incorporated any classifications of paediatric tumours. This decision has stemmed from the lack of an international standard staging system for many paediatric tumours. To enable stage data collection by population based cancer registries there needs to be agreement on cancer staging. Recognition of this led to a consensus meeting held in 2014.
and resulted in the publication of recommendations on the staging of paediatric malignancies for the purposes of population surveillance. The classifications published are not intended to replace the classifications used by the clinician when treating an individual patient but instead to facilitate the collection of stage by population-based cancer registries.

Related Classifications

Since 1958, WHO has been involved in a programme aimed at providing internationally acceptable criteria for the histological diagnosis of tumours. This has resulted in the International Histological Classification of Tumours, which contains, in an illustrated multivolume series, definitions of tumour types and a proposed nomenclature. A new series, WHO Classification of Tumours – Pathology and Genetics of Tumours, continues this effort. (Information on these publications is at www.iarc.fr).

The WHO International Classification of Diseases for Oncology (ICD O 3) is a coding system for neoplasms by topography and morphology and for indicating behaviour (e.g., malignant, benign). This coded nomenclature is identical in the morphology field for neoplasms to the Systematized Nomenclature of Medicine (SNOMED).

In the interest of promoting national and international collaboration in cancer research and specifically of facilitating cooperation in clinical investigations, it is recommended that the WHO Classification of Tumours be used for classification and definition of tumour types and that the ICD.O.3 code be used for storage and retrieval of data.

References


7 International Union Against Cancer (UICC). TNM Classification of Malignant


**Substantial changes in the 2016 eighth edition compared to the 2009 seventh edition are marked by a bar at the left-hand side of the page.**
Head and Neck Tumours

Introductory Notes

The following sites are included:

- Lip and oral cavity
- Pharynx: oropharynx (p16 negative and p16 positive), nasopharynx, hypopharynx
- Larynx: supraglottis, glottis, subglottis
- Nasal cavity and paranasal sinuses (maxillary and ethmoid sinus)
- Unknown primary carcinoma – cervical nodes
- Malignant melanoma of upper aerodigestive tract
- Major salivary glands
- Thyroid gland

Carcinomas arising in minor salivary glands of the upper aerodigestive tract are classified according to the rules for tumours of their anatomic site of origin, e.g., oral cavity.

**Each site is described under the following headings:**

- Rules for classification with the procedures for assessing T, N, and M categories; additional methods may be used when they enhance the accuracy of appraisal before treatment
- Anatomical sites and subsites where appropriate
- Definition of the regional lymph nodes
- TNM clinical classification
- pTNM pathological classification
- Stage
- Prognostic factors grid.

**Regional Lymph Nodes**

Midline nodes are considered ipsilateral nodes except in the thyroid.

**Lip and Oral Cavity**

(ICD-O-3 C00, C02-006)

**Rules for Classification**
The classification applies only to carcinomas of the vermilion surfaces of the lips and of the oral cavity, including those of minor salivary glands. There should be histological confirmation of the disease.

The following are the procedures for assessing T, N, and M categories:

- **T categories**  Physical examination and imaging
- **N categories**  Physical examination and imaging
- **M categories**  Physical examination and imaging

### Anatomical Sites and Subsites

#### Lip (C00)
1. External upper lip (vermilion border) (C00.0)
2. External lower lip (vermilion border) (C00.1)
3. Commissures (C00.6)

#### Oral Cavity (CO2–006)
1. Buccal mucosa
   - a. Mucosa of upper and lower lips (C00.3, 4)
   - b. Cheek mucosa (C06.0)
   - c. Retromolar areas (C06.2)
   - d. Buccoalveolar sulci, upper and lower (vestibule of mouth) (C06.1)
2. Upper alveolus and gingiva (upper gum) (C03.0)
3. Lower alveolus and gingiva (lower gum) (C03.14.
4. Hard palate (C05.0)
5. Tongue
   - a. Dorsal surface and lateral borders anterior to vallate papillae (anterior two-thirds) (C02.0, 1)
   - b. Inferior (ventral) surface (C02.2)
6. Floor of mouth (C04)

### Regional Lymph Nodes
The regional lymph nodes are the cervical nodes.

### TNM Clinical Classification
T – Primary Tumour

TX Primary tumour cannot be assessed
To No evidence of primary tumour
Tis Carcinoma in situ

T1 Tumour 2 cm or less in greatest dimension and 5 mm or less depth of invasion*

T2 Tumour 2 cm or less in greatest dimension and more than 5 mm but no more than 10 mm depth of invasion or Tumour more than 2 cm but not more than 4 cm in greatest dimension and depth of invasion no more than 10 mm

T3 Tumour more than 4 cm in greatest dimension or more than 10 mm depth of invasion

T4a (Lip) Tumour invades through cortical bone, inferior alveolar nerve, floor of mouth, or skin (of the chin or the nose)

T4a (Oral cavity) Tumour invades through the cortical bone of the mandible or maxillary sinus, or invades the skin of the face

T4b (Lip and oral cavity) Tumour invades masticator space, pterygoid plates, or skull base, or encases internal carotid artery

Note
* Superficial erosion alone of bone/tooth socket by gingival primary is not sufficient to classify a tumour as T4a.

N – Regional Lymph Nodes

NX Regional lymph nodes cannot be assessed
No No regional lymph node metastasis

N1 Metastasis in a single ipsilateral lymph node, 3 cm or less in greatest dimension without extranodal extension

N2 Metastasis described as:

N2a Metastasis in a single ipsilateral lymph node, more than 3 cm but not more than 6 cm in greatest dimension without extranodal extension

N2b Metastasis in multiple ipsilateral lymph nodes, none more than 6 cm in greatest dimension, without extranodal extension

N2c Metastasis in bilateral or contralateral lymph nodes, none more than 6 cm in greatest dimension, without extranodal extension

N3a Metastasis in a lymph node more than 6 cm in greatest dimension without extranodal extension

N3b Metastasis in a single or multiple lymph nodes with clinical extranodal extension*
Notes

The presence of skin involvement or soft tissue invasion with deep fixation/tethering to underlying muscle or adjacent structures or clinical signs of nerve involvement is classified as clinical extranodal extension.

Midline nodes are considered ipsilateral nodes.

**M – Distant Metastasis**

- M0 No distant metastasis
- M1 Distant metastasis

**pTNM Pathological Classification**

The pT categories correspond to the clinical T categories. For pM see page 8.

**pN – Regional Lymph Nodes**

Histological examination of a selective neck dissection specimen will ordinarily include 10 or more lymph nodes. Histological examination of a radical or modified radical neck dissection specimen will ordinarily include 15 or more lymph nodes.

- pNX Regional lymph nodes cannot be assessed
- pN0 No regional lymph node metastasis
- pN1 Metastasis in a single ipsilateral lymph node, 3 cm or less in greatest dimension without extranodal extension
- pN2 Metastasis described as:
  - pN2a Metastasis in a single ipsilateral lymph node, less than 3 cm in greatest dimension with extranodal extension or, more than 3 cm but not more than 6 cm in greatest dimension without extranodal extension
  - pN2b Metastasis in multiple ipsilateral lymph nodes, none more than 6 cm in greatest dimension, without extranodal extension
  - pN2c Metastasis in bilateral or contralateral lymph nodes, none more than 6 cm in greatest dimension, without extranodal extension
- pN3a Metastasis in a lymph node more than 6 cm in greatest dimension without extranodal extension
- pN3b Metastasis in a lymph node more than 3 cm in greatest dimension with extranodal extension or, multiple ipsilateral, or any contralateral or bilateral node(s) with extranodal extension

**Stage**

Stage 0 Tis N0 M0
Stage I  
T1  
N0  
M0

Stage II  
T2  
N0  
M0

Stage III  
T3  
N0  
M0

Stage IVA  
T4a  
N0, N1  
M0

Stage IVB  
Any T  
N3  
M0

Stage IVC  
Any T  
Any N  
M1

Prognostic Factors Grid – Oral Cavity

Prognostic factors for carcinoma of the oral cavity

<table>
<thead>
<tr>
<th>Prognostic factors</th>
<th>Tumour related</th>
<th>Host related</th>
<th>Environment related</th>
</tr>
</thead>
<tbody>
<tr>
<td>Essential</td>
<td>T category N category Extracapsular extension (ECE) Surgical resection margin</td>
<td>Performance status Addictions (tobacco/areca nut/alcohol)</td>
<td>Dose of radiotherapy/chemoradiotherapy</td>
</tr>
<tr>
<td>Additional</td>
<td>Tumour volume Hypoxia</td>
<td>Age Co.morbidity</td>
<td>Overall treatment/radiation treatment time Interval from surgery to start of postoperative radiotherapy</td>
</tr>
<tr>
<td>New and promising</td>
<td>EGFR expression  \textit{TP53} mutation  \textit{Bcl 2 ERCC1}</td>
<td>Swallowing. related quality of life Global quality of life</td>
<td></td>
</tr>
</tbody>
</table>


Pharynx

(ICD-O-3 C01, C05.1-2, C09, C10.0, 2-3, C11-13)

Rules for Classification

The classification applies only to carcinomas. There should be histological confirmation of the disease.
Changes to the seventh edition for carcinoma of the nasopharynx and the introduction of a separate classification for p16 positive oropharyngeal cancer are based on the recommendations referenced.¹ ² 

The following are the procedures for assessing T, N, and M categories:

- **T categories**  
  Physical examination, endoscopy and imaging

- **N categories**  
  Physical examination and imaging

- **M categories**  
  Physical examination and imaging

### Anatomical Sites and Subsites

#### Oropharynx (ICD-O 3 C01, C05.1 2, C09.0 1, 9, C10.0, 2 3)

1. Anterior wall (glossoepiglottic area)
   a. Base of tongue (posterior to the vallate papillae or posterior third) (C01)
   b. Vallecula (C10.0)
2. Lateral wall (C10.2)
   a. Tonsil (C09.9)
   b. Tonsillar fossa (C09.0) and tonsillar (faucial) pillars (C09.1)
   c. Glossotonsillar sulci (tonsillar pillars) (C09.1)
3. Posterior wall (C10.3)
4. Superior wall
   a. Inferior surface of soft palate (CO5.1)
   b. Uvula (CO5.2)

#### Nasopharynx (C11)

1. Posterosuperior wall: extends from the level of the junction of the hard and soft palates to the base of the skull (C11.0, 1)
2. Lateral wall: including the fossa of Rosenmüller (C11.2)
3. Inferior wall: consists of the superior surface of the soft palate (C11.3)

**Note**

The margin of the choanal orifices, including the posterior margin of the nasal septum, is included with the nasal fossa.

#### Hypopharynx (C12, C13)

1. Pharyngoesophageal junction (postcricoid area) (C13.0): extends from the level of
the arytenoid cartilages and connecting folds to the inferior border of the cricoid cartilage, thus forming the anterior wall of the hypopharynx

2. Piriform sinus (C12.9): extends from the pharyngoepiglottic fold to the upper end of the oesophagus. It is bounded laterally by the thyroid cartilage and medially by the hypopharyngeal surface of the aryepiglottic fold (C13.1) and the arytenoid and cricoid cartilages

3. Posterior pharyngeal wall (C13.2): extends from the superior level of the hyoid bone (or floor of the vallecula) to the level of the inferior border of the cricoid cartilage and from the apex of one piriform sinus to the other

Regional Lymph Nodes
The regional lymph nodes are the cervical nodes.

TNM Clinical Classification

T – Primary Tumour

TX Primary tumour cannot be assessed
T0 No evidence of primary tumour
Tis Carcinoma in situ

Oropharynx

p16-negative cancers of the oropharynx or oropharyngeal cancers without a p16 immunohistochemistry performed.

T1 Tumour 2 cm or less in greatest dimension
T2 Tumour more than 2 cm but not more than 4 cm in greatest dimension
T3 Tumour more than 4 cm in greatest dimension or extension to lingual surface of epiglottis
T4a Tumour invades any of the following: larynx,* deep/extrinsic muscle of tongue (genioglossus, hyoglossus, palatoglossus, and styloglossus), medial pterygoid, hard palate, or mandible
T4b Tumour invades any of the following: lateral pterygoid muscle, pterygoid plates, lateral nasopharynx, skull base; or encases carotid artery

Note

* Mucosal extension to lingual surface of epiglottis from primary tumours of the base of the tongue and vallecula does not constitute invasion of the larynx.

Oropharynx – p16-Positive Tumours
Tumours that have positive p16 immunohistochemistry overexpression.

**T1** Tumour 2.0 cm or less in greatest dimension

**T2** Tumour more than 2.0 cm but not more than 4.0 cm in greatest dimension

**T3** Tumour more than 4.0 cm in greatest dimension or extension to lingual surface of epiglottis

**T4** Tumour invades any of the following: larynx*, deep/extrinsic muscle of tongue (genioglossus, hyoglossus, palatoglossus, and styloglossus), medial pterygoid, hard palate, mandible*, lateral pterygoid muscle, pterygoid plates, lateral nasopharynx, skull base; or encases carotid artery

**Note**

* Mucosal extension to lingual surface of epiglottis from primary tumours of the base of the tongue and vallecula does not constitute invasion of the larynx.

**Hypopharynx**

**T1** Tumour limited to one subsite of hypopharynx (see page 23 and/or 2.0 cm or less in greatest dimension

**T2** Tumour invades more than one subsite of hypopharynx or an adjacent site, or measures more than 2.0 cm but not more than 4.0 cm in greatest dimension, *without* fixation of hemilarynx

**T3** Tumour more than 4.0 cm in greatest dimension, or *with* fixation of hemilarynx or extension to oesophagus

**T4a** Tumour invades any of the following: thyroid/cricoid cartilage, hyoid bone, thyroid gland, oesophagus, central compartment soft tissue*

**T4b** Tumour invades prevertebral fascia, encases carotid artery, or invades mediastinal structures

**Note**

* Central compartment soft tissue includes prelaryngeal strap muscles and subcutaneous fat.

**Nasopharynx**

**T1** Tumour confined to nasopharynx, or extends to oropharynx and/or nasal cavity *without* parapharyngeal involvement

**T2** Tumour with extension to parapharyngeal space and/or infiltration of the medial pterygoid, lateral pterygoid, and/or prevertebral muscles

**T3** Tumour invades bony structures of skull base cervical vertebra, pterygoid structures, and/or paranasal sinuses
T4 Tumour with intracranial extension and/or involvement of cranial nerves, hypopharynx, orbit, parotid gland and/or infiltration beyond the lateral surface of the lateral pterygoid muscle

N – Regional Lymph Nodes

**Oropharynx – p16- Negative and Hypopharynx**

NX Regional lymph nodes cannot be assessed

No No regional lymph node metastasis

N1 Metastasis in a single ipsilateral lymph node, 3.cm or less in greatest dimension without extranodal extension

N2 Metastasis described as:

N2a Metastasis in a single ipsilateral lymph node more than 3.cm but not more than 6.cm in greatest dimension without extranodal extension

N2b Metastasis in multiple ipsilateral lymph nodes, none more than 6.cm in greatest dimension, without extranodal extension

N2c Metastasis in bilateral or contralateral lymph nodes, none more than 6.cm in greatest dimension, without extranodal extension

N3a Metastasis in a lymph node more than 6.cm in greatest dimension without extranodal extension

N3b Metastasis in a single or multiple lymph nodes with clinical extranodal extension*

**Notes**

* The presence of skin involvement or soft tissue invasion with deep fixation/tethering to underlying muscle or adjacent structures or clinical signs of nerve involvement is classified as clinical extranodal extension.

Midline nodes are considered ipsilateral nodes.

**Oropharynx p- 16 Positive**

**Clinical**

NX Regional lymph nodes cannot be assessed

No No regional lymph node metastasis

N1 Unilateral metastasis, in lymph node(s), all 6.cm or less in greatest dimension

N2 Contralateral or bilateral metastasis in lymph node(s), all 6.cm or less in greatest dimension

N3 Metastasis in lymph node(s) greater than 6.cm in dimension
Note
Midline nodes are considered ipsilateral nodes.

**Nasopharynx**

NX Regional lymph nodes cannot be assessed
N0 No regional lymph node metastasis
N1 Unilateral metastasis, in cervical lymph node(s), and/or unilateral or bilateral metastasis in retropharyngeal lymph nodes, 6 cm or less in greatest dimension, above the caudal border of cricoid cartilage
N2 Bilateral metastasis in cervical lymph node(s), 6 cm or less in greatest dimension, above the caudal border of cricoid cartilage
N3 Metastasis in cervical lymph node(s) greater than 6 cm in dimension and/or extension below the caudal border of cricoid cartilage

Note
Midline nodes are considered ipsilateral nodes.

**M – Distant Metastasis**

M0 No distant metastasis
M1 Distant metastasis

**pTNM Pathological Classification**

The pT categories correspond to the T categories. For pM see page 8.

Histological examination of a selective neck dissection specimen will ordinarily include 10 or more lymph nodes. Histological examination of a radical or modified radical neck dissection specimen will ordinarily include 15 or more lymph nodes.

**Oropharynx – p16 Negative and Hypopharynx**

pNX Regional lymph nodes cannot be assessed
pN0 No regional lymph node metastasis
pN1 Metastasis in a single ipsilateral lymph node, 3 cm or less in greatest dimension without extranodal extension
pN2 Metastasis described as:
   pN2a Metastasis in a single ipsilateral lymph node, less than 3 cm in greatest dimension with extranodal extension or more than 3 cm but not more than 6 cm in greatest dimension without extranodal extension
   pN2b Metastasis in multiple ipsilateral lymph nodes, none more than 6 cm in
greatest dimension, without extranodal extension
pN2c Metastasis in bilateral or contralateral lymph nodes, none more than 6 cm in
greatest dimension, without extranodal extension
pN3a Metastasis in a lymph node more than 6 cm in greatest dimension without
extranodal extension
pN3b Metastasis in a lymph node more than 3 cm in greatest dimension with extranodal
extension or, multiple ipsilateral, or any contralateral or bilateral node(s) with
extranodal extension

Oropharynx p 16 Positive

pNX Regional lymph nodes cannot be assessed
pNo No regional lymph node metastasis
pN1 Metastasis in 1 to 4 lymph node(s)
pN2 Metastasis in 5 or more lymph node(s)

Nasopharynx
The pN categories correspond to the N categories

Stage (Oropharynx – p16 Negative and Hypopharynx)

Stage 0 Tis No Mo
Stage I T1 No Mo
Stage II T2 No Mo
Stage III T3 No Mo
T1, T2, T3 N1 Mo
Stage IVA T1, T2, T3 N2 Mo
T4a No, N1, N2 Mo
Stage IVB T4b Any N Mo
Any T N3 Mo
Stage IVC Any T Any N M1

Stage (Oropharynx – p16 Positive)

Clinical

Stage 0 Tis No Mo
Stage I T1, T2 No, N1 Mo
Stage II T1, T2 N2 Mo
T3 No, N1, N2 Mo
Stage III  
T1, T2, T3 N3  Mo  
T4  Any  Mo  
Stage IV  Any T  Any N  M1

Pathological

Stage 0  Tis  No  Mo  
Stage I  T1, T2 No, 1  Mo  
Stage II  T1, T2 N2  Mo  
T3  No, N1 Mo  
Stage III  T3, T4 N2  Mo  
Stage IV  Any T  Any N  M1

Stage (Nasopharynx)

Stage 0  Tis  No  Mo  
Stage I  T1  No  Mo  
Stage II  T1  N1  Mo  
T2  No, N1  Mo  
Stage III  T1, T2 N2  Mo  
T3  No, N1, N2  Mo  
Stage IVA  T4  No, N1, N2  Mo  
Stage IVA  Any T  N3  Mo  
Stage IVB  Any T  Any N  M1

Prognostic Factors Grid

Oropharynx


### Prognostic risk factors for survival of OPC

<table>
<thead>
<tr>
<th>Prognostic factors</th>
<th>Tumour related</th>
<th>Host related</th>
<th>Environment related</th>
</tr>
</thead>
<tbody>
<tr>
<td>Essential</td>
<td>HPV status (including p16) T category N category</td>
<td>Smoking, especially during radiotherapy Performance status</td>
<td>Quality of treating facility (staging workup and expertise in multidisciplinary management)</td>
</tr>
</tbody>
</table>
|                    | Number of involved nodes Level of involved nodes Tumour volume Hypoxia | Co.morbidities Age | Ability to receive standard treatment:  
  - Radiation dose  
  - Overall treatment time  
  - Quality of radiotherapy |
| New and promising  | EGFR expression TP53 mutation Bcl 2 ERCC1 | Health related quality of life | |


### Nasopharynx

Prognostic factors for nasopharyngeal carcinoma

<table>
<thead>
<tr>
<th>Prognostic factors</th>
<th>Tumour related</th>
<th>Host related</th>
<th>Environment related</th>
</tr>
</thead>
<tbody>
<tr>
<td>Essential</td>
<td>Presenting stage Histological type</td>
<td>Age</td>
<td>Facilities for staging work up (MRI, PET, CT)Facilities for high quality radiotherapy (conformal techniques and precision)Appropriate addition of chemotherapy Expertise in radiotherapy and chemotherapy</td>
</tr>
<tr>
<td>Additional</td>
<td>EBV, DNA Gross tumour volume Site of metastases</td>
<td>LDH</td>
<td>Optimization of radiotherapy dose fractionation Optimization of chemotherapy sequence and drugs</td>
</tr>
<tr>
<td>New and promising</td>
<td>Biomarkers Gene signatures</td>
<td>Advances in diagnostic and therapeutic technology</td>
<td></td>
</tr>
</tbody>
</table>

References


Larynx

(ICD-O-3 C32.0-2, C10.1)

Rules for Classification

The classification applies only to carcinomas. There should be histological confirmation of the disease.

The following are the procedures for assessing T, N, and M categories:

- **T categories**  Physical examination, laryngoscopy, and imaging
- **N categories**  Physical examination and imaging
- **M categories**  Physical examination and imaging

Anatomical Sites and Subsites

1. Supraglottis (C32.1)
   - a. Suprahypoid epiglottis [including tip, lingual (anterior) (C 10.1), and laryngeal surfaces]
   - b. Aryepiglottic fold, laryngeal aspect
   - c. Arytenoid
   - d. Infrahypoid epiglottis
   - e. Ventricular bands (false cords)

   \[
   \text{Epilarynx (including marginal zone)} \]

2. Glottis (C32.0)
   - a. Vocal cords
   - b. Anterior commissure
   - c. Posterior commissure

3. Subglottis (C32.2)

Regional Lymph Nodes
The regional lymph nodes are the cervical nodes.

**TNM Clinical Classification**

**T – Primary Tumour**

- **TX**: Primary tumour cannot be assessed
- **T0**: No evidence of primary tumour
- **Tis**: Carcinoma in situ

**Supraglottis**

- **T1**: Tumour limited to one subsite of supraglottis with normal vocal cord mobility
- **T2**: Tumour invades mucosa of more than one adjacent subsite of supraglottis or glottis or region outside the supraglottis (e.g., mucosa of base of tongue, vallecula, medial wall of piriform sinus) without fixation of the larynx
- **T3**: Tumour limited to larynx with vocal cord fixation and/or invades any of the following: postcricoid area, pre.epiglottic space, paraglottic space, and/or inner cortex of thyroid cartilage
- **T4a**: Tumour invades through the thyroid cartilage and/or invades tissues beyond the larynx, e.g., trachea, soft tissues of neck including deep/extrinsic muscle of tongue (genioglossus, hyoglossus, palatoglossus, and styloglossus), strap muscles, thyroid, or oesophagus
- **T4b**: Tumour invades prevertebral space, encases carotid artery, or mediastinal structures

**Glottis**

- **T1**: Tumour limited to vocal cord(s) (may involve anterior or posterior commissure) with normal mobility
  - **T1a**: Tumour limited to one vocal cord
  - **T1b**: Tumour involves both vocal cords
- **T2**: Tumour extends to supraglottis and/or subglottis, and/or with impaired vocal cord mobility
- **T3**: Tumour limited to larynx with vocal cord fixation and/or invades paraglottic space, and/or inner cortex of the thyroid cartilage
- **T4a**: Tumour invades through the outer cortex of the thyroid cartilage, and/or invades tissues beyond the larynx, e.g., trachea, soft tissues of neck including deep/extrinsic muscle of tongue (genioglossus, hyoglossus, palatoglossus, and styloglossus), strap muscles, thyroid, oesophagus
- **T4b**: Tumour invades prevertebral space, encases carotid artery, or mediastinal structures

**Subglottis**
T1  Tumour limited to subglottis
T2  Tumour extends to vocal cord(s) with normal or impaired mobility
T3  Tumour limited to larynx with vocal cord fixation
T4a Tumour invades cricoid or thyroid cartilage and/or invades tissues beyond the larynx, e.g., trachea, soft tissues of neck including deep/extrinsic muscle of tongue (genioglossus, hyoglossus, pala toglossus, and styloglossus), strap muscles, thyroid, oesophagus
T4b Tumour invades prevertebral space, encases carotid artery, or mediastinal structures

N – Regional Lymph Nodes
N1  Metastasis in a single ipsilateral lymph node, 3 cm or less in greatest dimension without extranodal extension
N2  Metastasis described as:
   N2a Metastasis in a single ipsilateral lymph node, more than 3 cm but not more than 6 cm in greatest dimension without extranodal extension
   N2b Metastasis in multiple ipsilateral lymph nodes, none more than 6 cm in greatest dimension, without extranodal extension
   N2c Metastasis in bilateral or contralateral lymph nodes, none more than 6 cm in greatest dimension, without extranodal extension
N3a Metastasis in a lymph node more than 6 cm in greatest dimension without extranodal extension
N3b Metastasis in a single or multiple lymph nodes with clinical extranodal extension

Notes
* The presence of skin involvement or soft tissue invasion with deep fixation/tethering to underlying muscle or adjacent structures or clinical signs of nerve involvement is classified as clinical extranodal extension.
Midline nodes are considered ipsilateral nodes.

M – Distant Metastasis
M0  No distant metastasis
M1  Distant metastasis

pTNM Pathological Classification
The pT categories correspond to the clinical T categories. For pM see page 8.

pN – Regional Lymph Nodes
Histological examination of a selective neck dissection specimen will ordinarily include 10 or more lymph nodes. Histological examination of a radical or modified radical neck dissection specimen will ordinarily include 15 or more lymph nodes.

pNX  Regional lymph nodes cannot be assessed
pN0  No regional lymph node metastasis
pN1  Metastasis in a single ipsilateral lymph node, 3.cm or less in greatest dimension without extranodal extension
pN2  Metastasis described as:
   pN2a Metastasis in a single ipsilateral lymph node, less than 3.cm in greatest dimension with extranodal extension or more than 3.cm but not more than 6.cm in greatest dimension without extranodal extension
   pN2b Metastasis in multiple ipsilateral lymph nodes, none more than 6.cm in greatest dimension, without extranodal extension
   pN2c Metastasis in bilateral or contralateral lymph nodes, none more than 6.cm in greatest dimension, without extranodal extension
pN3a Metastasis in a lymph node more than 6.cm in greatest dimension without extranodal extension
pN3b Metastasis in a lymph node more than 3.cm in greatest dimension with extranodal extension or multiple ipsilateral, or any contralateral or bilateral node(s) with extranodal extension

Stage

<table>
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<tr>
<th>Stage</th>
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<th>T1</th>
<th>T2</th>
<th>T3</th>
<th>T1,T2,T3</th>
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<th>T4b</th>
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<td>Mo</td>
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Prognostic factors for survival for laryngeal and hypopharyngeal carcinoma

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<th>Environment related</th>
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<tr>
<td>Essential</td>
<td>T, N, M categories Extracapsular extension</td>
<td>Co. morbidities Age &gt;70 years Performance status</td>
<td>Able to provide standard treatment (resources) Treatment quality Resection margins</td>
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<td>Additional</td>
<td>Regions/subsites involved Low neck nodes Tumour volume Vocal cord impairment Tracheostomy</td>
<td>Gender Laryngeal function</td>
<td>Nutrition Social/environmental (e.g. anatomical station) Overall treatment time</td>
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<td>New and promising</td>
<td>Tumour markers: TP53, VEGF, cyclin D1 amplification, EGFR, Bcl 2 Tumour HPV status Chemoresistance genes</td>
<td>Baseline quality of life</td>
<td>Optical imaging New sensitizers in photodynamic therapy</td>
</tr>
</tbody>
</table>


Nasal Cavity and Paranasal Sinuses

(ICD-O-3 C30.0, 31.0-1)

Rules for Classification

The classification applies only to carcinomas. There should be histological confirmation of the disease.

The following are the procedures for assessing T, N, and M categories:

- **T categories** Physical examination and imaging
- **N categories** Physical examination and imaging
- **M categories** Physical examination and imaging

Anatomical Sites and Subsites

1. Nasal cavity (C30.0)
   - Septum
   - Floor
   - Lateral wall
2. Maxillary sinus (C31.0)
3. Ethmoid sinus (C31.1)
   - Left
   - Right

**Regional Lymph Nodes**
The regional lymph nodes are the cervical nodes.

**TNM Clinical Classification**

**T – Primary Tumour**

- **TX** Primary tumour cannot be assessed
- **T0** No evidence of primary tumour
- **Tis** Carcinoma in situ

**Maxillary Sinus**

- **T1** Tumour limited to the mucosa with no erosion or destruction of bone
- **T2** Tumour causing bone erosion or destruction, including extension into the hard palate and/or middle nasal meatus, except extension to posterior wall of maxillary sinus and pterygoid plates
- **T3** Tumour invades any of the following: bone of posterior wall of maxillary sinus, subcutaneous tissues, floor or medial wall of orbit, pterygoid fossa, or ethmoid sinuses
- **T4a** Tumour invades any of the following: anterior orbital contents, skin of cheek, pterygoid plates, infratemporal fossa, cribiform plate, sphenoid or frontal sinuses
- **T4b** Tumour invades any of the following: orbital apex, dura, brain, middle cranial fossa, cranial nerves other than maxillary division of trigeminal nerve (V2), nasopharynx, or clivus

**Nasal Cavity and Ethmoid Sinus**

- **T1** Tumour restricted to one subsite of nasal cavity or ethmoid sinus, with or without bony invasion
- **T2** Tumour involves two subsites in a single site or extends to involve an adjacent site within the nasoethmoidal complex, with or without bony invasion
- **T3** Tumour extends to invade the medial wall or floor of the orbit, maxillary sinus, palate, or cribiform plate
- **T4a** Tumour invades any of the following: anterior orbital contents, skin of nose or...
cheek, minimal extension to anterior cranial fossa, pterygoid plates, sphenoid or frontal sinuses

T4b Tumour invades any of the following: orbital apex, dura, brain, middle cranial fossa, cranial nerves other than V2, nasopharynx, or clivus

N – Regional Lymph Nodes

N1 Metastasis in a single ipsilateral lymph node, 3 cm or less in greatest dimension without extranodal extension

N2 Metastasis described as:
   N2a Metastasis in a single ipsilateral lymph node, more than 3 cm but not more than 6 cm in greatest dimension without extranodal extension
   N2b Metastasis in multiple ipsilateral lymph nodes, none more than 6 cm in greatest dimension, without extranodal extension
   N2c Metastasis in bilateral or contralateral lymph nodes, none more than 6 cm in greatest dimension, without extranodal extension

N3a Metastasis in a lymph node more than 6 cm in greatest dimension without extranodal extension

N3b Metastasis in a single or multiple lymph nodes with clinical extranodal extension

Notes

* The presence of skin involvement or soft tissue invasion with deep fixation/tethering to underlying muscle or adjacent structures or clinical signs of nerve involvement is classified as clinical extra nodal extension.

Midline nodes are considered ipsilateral nodes.

M – Distant Metastasis

   M0 No distant metastasis
   M1 Distant metastasis

pTNM Pathological Classification

The pT categories correspond to the clinical T categories. For pM see page 8.

pN – Regional Lymph Nodes

Histological examination of a selective neck dissection specimen will ordinarily include 10 or more lymph nodes. Histological examination of a radical or modified radical neck dissection specimen will ordinarily include 15 or more lymph nodes.

pNX Regional lymph nodes cannot be assessed
**pN0**  No regional lymph node metastasis

**pN1**  Metastasis in a single ipsilateral lymph node, 3. cm or less in greatest dimension without extranodal extension

**pN2**  Metastasis described as:

- **pN2a**  Metastasis in a single ipsilateral lymph node, less than 3. cm in greatest dimension with extranodal extension or, more than 3. cm but not more than 6. cm in greatest dimension without extranodal extension

- **pN2b**  Metastasis in multiple ipsilateral lymph nodes, none more than 6. cm in greatest dimension, without extranodal extension

- **pN2c**  Metastasis in bilateral or contralateral lymph nodes, none more than 6. cm in greatest dimension, without extranodal extension

**pN3a**  Metastasis in a lymph node more than 6. cm in greatest dimension without extranodal extension

**pN3b**  Metastasis in a lymph node more than 3. cm in greatest dimension with extranodal extension or multiple ipsilateral, or any contralateral or bilateral node(s) with extranodal extension

### Stage

<table>
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<tr>
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<tbody>
<tr>
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<tr>
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<tr>
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<td>T1, T2, T3 N1</td>
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<td>Stage IVA</td>
<td>T1, T2, T3 N2</td>
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<tr>
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<td>T4a</td>
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<td>Stage IVB</td>
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<td>Stage IVC</td>
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<td>Any N</td>
<td>M1</td>
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**Prognostic Factors Grid – Nasal Cavity and Paranasal Sinuses**
Prognostic factors for paranasal sinus tumours

<table>
<thead>
<tr>
<th>Prognostic factors</th>
<th>Tumour related</th>
<th>Host related</th>
<th>Environment related</th>
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<tbody>
<tr>
<td>Essential</td>
<td>T category</td>
<td>N category</td>
<td>M category</td>
</tr>
<tr>
<td>Additional</td>
<td>Histotype</td>
<td>Age Gender</td>
<td>Radiation dose</td>
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<td>Performance</td>
<td>Overall treatment time</td>
</tr>
<tr>
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<td>status</td>
<td>Surgical margins</td>
</tr>
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<td>New and promising</td>
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<td>High precision optimal dose radiation</td>
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<tr>
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<td></td>
<td>Concurrent cytotoxic or biological therapies</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Ideal integration with advanced surgical techniques</td>
</tr>
</tbody>
</table>


Unknown Primary – Cervical Nodes

Rules for Classification

There should be histological confirmation of squamous cell carcinoma with lymph node metastases but without an identified primary carcinoma. Histological methods should be used to identify EBV and HPV/p16-related tumours. If there is evidence of EBV, the nasopharyngeal classification is applied. If there is evidence of HPV and positive immunohistochemistry p16 overexpression, the p16-positive oropharyngeal classification is applied.

TNM Clinical Classification

*EBV or HPV/p16 negative or unknown*

T – Primary Tumour

To No evidence of primary tumour

N – Regional Lymph Nodes

N1 Metastasis in a single ipsilateral lymph node, 3 cm or less in greatest dimension without extranodal extension

N2 Metastasis described as:
N2a Metastasis in a single ipsilateral lymph node, more than 3 cm but not more than 6 cm in greatest dimension without extranodal extension

N2b Metastasis in multiple ipsilateral lymph nodes, none more than 6 cm in greatest dimension, without extranodal extension

N2c Metastasis in bilateral or contralateral lymph nodes, none more than 6 cm in greatest dimension, without extranodal extension

N3a Metastasis in a lymph node more than 6 cm in greatest dimension without extranodal extension

N3b Metastasis in a single or multiple lymph nodes with clinical extranodal extension*

Notes

* The presence of skin involvement or soft tissue invasion with deep fixation/tethering to underlying muscle or adjacent structures or clinical signs of nerve involvement is classified as clinical extranodal extension.

Midline nodes are considered ipsilateral nodes.

M – Distant Metastasis

M0 No distant metastasis
M1 Distant metastasis

pTNM Pathological Classification

The pT category corresponds to the clinical T category.

For pM see page 8.

pN – Regional Lymph Nodes

Histological examination of a selective neck dissection specimen will ordinarily include 10 or more lymph nodes. Histological examination of a radical or modified radical neck dissection specimen will ordinarily include 15 or more lymph nodes.

pN1 Metastasis in a single ipsilateral lymph node, 3 cm or less in greatest dimension without extranodal extension

pN2 Metastasis described as:

pN2a Metastasis in a single ipsilateral lymph node, less than 3 cm in greatest dimension with extranodal extension or more than 3 cm but not more than 6 cm in greatest dimension without extranodal extension

pN2b Metastasis in multiple ipsilateral lymph nodes, none more than 6 cm in greatest dimension, without extranodal extension

pN2c Metastasis in bilateral or contralateral lymph nodes, none more than 6 cm in
greatest dimension, without extranodal extension

pN3a Metastasis in a lymph node more than 6. cm in greatest dimension without extranodal extension

pN3b Metastasis in a lymph node more than 3. cm in greatest dimension with extranodal extension or multiple ipsilateral, or any contralateral, or bilateral node(s) with extranodal extension

Stage

<table>
<thead>
<tr>
<th>Stage</th>
<th>T</th>
<th>N</th>
<th>M</th>
</tr>
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<tbody>
<tr>
<td>III</td>
<td>T0</td>
<td>N1</td>
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</tr>
<tr>
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<td>IVC</td>
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<td>N1, N2, N3</td>
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</tbody>
</table>

TNM Clinical Classification

HPV/p16 positive

T – Primary Tumour

To No evidence of primary tumour

N – Regional Lymph Nodes

N1 Unilateral metastasis, in cervical lymph node(s), all 6 cm or less in greatest dimension

N2 Contralateral or bilateral metastasis in cervical lymph node(s), all 6 cm or less in greatest dimension

N3 Metastasis in cervical lymph node(s) greater than 6 cm in dimension

pTNM Pathological Classification

There is no pT category.

pN – Regional Lymph Nodes

Histological examination of a selective neck dissection specimen will ordinarily include 10 or more lymph nodes. Histological examination of a radical or modified radical neck dissection specimen will ordinarily include 15 or more lymph nodes.

pN1 Metastasis in 1 to 4 lymph node(s)

pN2 Metastasis in 5 or more lymph node(s)
**Stage**

*Clinical*

<table>
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<th>Stage</th>
<th>T</th>
<th>N</th>
<th>M</th>
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*Pathological*

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<tr>
<td>IV</td>
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<td>1, 2</td>
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</table>

**TNM Clinical Classification**

*EBV positive*

**T – Primary Tumour**

To No evidence of primary tumour

**N – Regional Lymph Nodes (Nasopharynx)**

N1 Unilateral metastasis, in cervical lymph node(s), and/or unilateral or bilateral metastasis in retropharyngeal lymph nodes, 6 cm or less in greatest dimension, above the caudal border of cricoid cartilage

N2 Bilateral metastasis in cervical lymph node(s), 6 cm or less in greatest dimension, above the caudal border of cricoid cartilage

N3 Metastasis in cervical lymph node(s) greater than 6 cm in dimension and/or extension below the caudal border of cricoid cartilage

**Note**

Midline nodes are considered ipsilateral nodes.

**pTNM Pathological Classification**

The pT and pN categories correspond to the T and N categories. For pM see page 8.

pN0 Histological examination of a selective neck dissection specimen will ordinarily include 10 or more lymph nodes. Histological examination of a radical or modified radical neck dissection specimen will ordinarily include 15 or more lymph nodes.
Malignant Melanoma of Upper Aerodigestive Tract

(ICD-O-3 C00-06, 10-14, 30-32)

Rules for Classification

The classification applies only to mucosal malignant melanomas of the head and neck region, i.e., of the upper aerodigestive tract. There should be histological confirmation of the disease and division of cases by site.
The following are the procedures for assessing T, N, and M categories:

**T categories**  
Physical examination and imaging

**N categories**  
Physical examination and imaging

**M categories**  
Physical examination and imaging

### Regional Lymph Nodes

The regional lymph nodes are those appropriate to the site of the primary tumour. See page 17.

### TNM Clinical Classification

#### T – Primary Tumour

- **TX** Primary tumour cannot be assessed
- **T0** No evidence of primary tumour
- **T3** Tumour limited to the epithelium and/or submucosa (mucosal disease)
- **T4a** Tumour invades deep soft tissue, cartilage, bone, or overlying skin
- **T4b** Tumour invades any of the following: brain, dura, skull base, lower cranial nerves (IX, X, XI, XII), masticator space, carotid artery, prevertebral space, mediastinal structures

**Note**

Mucosal melanomas are aggressive tumours, therefore T1 and T2 are omitted as are stages I and II.

#### N – Regional Lymph Nodes

- **NX** Regional lymph nodes cannot be assessed
- **N0** No regional lymph node metastasis
- **N1** Regional lymph node metastasis

#### M – Distant Metastasis

- **M0** No distant metastasis
- **M1** Distant metastasis

### pTNM Pathological Classification

The pT and pN categories correspond to the T and N categories. For pM see page 8.

pNo Histological examination of a regional lymphadenectomy specimen will ordinarily
include 6 or more lymph nodes. If the lymph nodes are negative, but the number ordinarily examined is not met, classify as pN0.

Stage

<table>
<thead>
<tr>
<th>Stage</th>
<th>T</th>
<th>N</th>
<th>M</th>
</tr>
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<tbody>
<tr>
<td>Stage III</td>
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<td>Stage IVC</td>
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<td>Any N</td>
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Major Salivary Glands

(ICD-O-3 C07, C08)

Rules for Classification

The classification applies only to carcinomas of the major salivary glands. Tumours arising in minor salivary glands (mucus secreting glands in the lining membrane of the upper aerodigestive tract) are not included in this classification but at their anatomic site of origin, e.g., lip. There should be histological confirmation of the disease.

The following are the procedures for assessing T, N, and M categories:

- **T categories**  Physical examination and imaging
- **N categories**  Physical examination and imaging
- **M categories**  Physical examination and imaging

Anatomical Sites

- Parotid gland (C07.9)
- Submandibular (submaxillary) gland (C08.0)
- Sublingual gland (C08.1)

Regional Lymph Nodes

The regional lymph nodes are the cervical nodes.

TNM Clinical Classification

**T – Primary Tumour**

TX Primary tumour cannot be assessed
T0  No evidence of primary tumour

T1  Tumour 2 cm or less in greatest dimension without extraparenchymal extension

T2  Tumour more than 2 cm but not more than 4 cm in greatest dimension without extraparenchymal extension

T3  Tumour more than 4 cm and/or tumour with extraparenchymal extension

T4a Tumour invades skin, mandible, ear canal, and/or facial nerve

T4b Tumour invades base of skull, and/or pterygoid plates, and/or encases carotid artery

Note

*Extraparenchymal extension is clinical or macroscopic evidence of invasion of soft tissues or nerve, except those listed under T4a and T4b. Microscopic evidence alone does not constitute extraparenchymal extension for classification purposes.

N – Regional Lymph Nodes

N1  Metastasis in a single ipsilateral lymph node, 3 cm or less in greatest dimension without extranodal extension

N2  Metastasis described as:

   N2a Metastasis in a single ipsilateral lymph node, more than 3 cm but not more than 6 cm in greatest dimension without extranodal extension

   N2b Metastasis in multiple ipsilateral lymph nodes, none more than 6 cm in greatest dimension, without extranodal extension

   N2c Metastasis in bilateral or contralateral lymph nodes, none more than 6 cm in greatest dimension, without extranodal extension

N3a Metastasis in a lymph node more than 6 cm in greatest dimension without extranodal extension

N3b Metastasis in a single or multiple lymph nodes with clinical extranodal extension

Notes

*The presence of skin involvement or soft tissue invasion with deep fixation/tethering to underlying muscle or adjacent structures or clinical signs of nerve involvement is classified as clinical extra nodal extension.

Midline nodes are considered ipsilateral nodes.

M – Distant Metastasis

Mo  No distant metastasis

M1  Distant metastasis
pTNM Pathological Classification

The pT categories correspond to the clinical T categories. For pM see page 8.

**pN – Regional Lymph Nodes**

Histological examination of a selective neck dissection specimen will ordinarily include 10 or more lymph nodes. Histological examination of a radical or modified radical neck dissection specimen will ordinarily include 15 or more lymph nodes.

- **pNX** Regional lymph nodes cannot be assessed
- **pN0** No regional lymph node metastasis
- **pN1** Metastasis in a single ipsilateral lymph node, 3 cm or less in greatest dimension without extranodal extension
- **pN2** Metastasis described as:
  - **pN2a** Metastasis in a single ipsilateral lymph node, less than 3 cm in greatest dimension with extranodal extension or, more than 3 cm but not more than 6 cm in greatest dimension without extranodal extension
  - **pN2b** Metastasis in multiple ipsilateral lymph nodes, none more than 6 cm in greatest dimension, without extranodal extension
  - **pN2c** Metastasis in bilateral or contralateral lymph nodes, none more than 6 cm in greatest dimension, without extranodal extension
- **pN3a** Metastasis in a lymph node more than 6 cm in greatest dimension without extranodal extension
- **pN3b** Metastasis in a lymph node more than 3 cm in greatest dimension with extranodal extension or multiple ipsilateral, or any contralateral, or bilateral node(s) with extranodal extension

**Stage**

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Prognostic Factors for Salivary Gland Tumour Survival

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<th>Environment Related</th>
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<td>Age</td>
<td>Resection margins and residual disease (R0/R1/R2)</td>
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<td>Local invasion</td>
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<td>Perineural invasion</td>
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<tr>
<td>Additional</td>
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<td>Facial palsy, pain</td>
<td>Adjuvant radiotherapy</td>
</tr>
<tr>
<td>New and promising</td>
<td>Molecular markers (c,Kit, Ki67, HER2, EGFR, VEGF, androgen receptors)</td>
<td>Neutron vs photon radiotherapy</td>
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Thyroid Gland (ICD-O-3 C73.9)

Rules for Classification

The classification applies only to carcinomas. There should be microscopic confirmation of the disease and division of cases by histological type.

The following are the procedures for assessing T, N, and M categories:

- **T categories**  Physical examination, endoscopy, and imaging
- **N categories**  Physical examination and imaging
- **M categories**  Physical examination and imaging

Regional Lymph Nodes

The regional lymph nodes are the cervical and upper/superior mediastinal nodes.

TNM Clinical Classification

**T – Primary Tumour**

TX Primary tumour cannot be assessed
No evidence of primary tumour

T1  Tumour 2 cm or less in greatest dimension, limited to the thyroid
    T1a Tumour 1 cm or less in greatest dimension, limited to the thyroid
    T1b Tumour more than 1 cm but not more than 2 cm in greatest dimension, limited to the thyroid

T2  Tumour more than 2 cm but not more than 4 cm in greatest dimension, limited to the thyroid

T3  Tumour more than 4 cm in greatest dimension, limited to the thyroid or with gross extrathyroidal extension invading only strap muscles (sternohyoid, sternothyroid, or omohyoid muscles)
    T3a Tumour more than 4 cm in greatest dimension, limited to the thyroid
    T3b Tumour of any size with gross extrathyroidal extension invading strap muscles (sternohyoid, sternothyroid, or omohyoid muscles)

T4a Tumour extends beyond the thyroid capsule and invades any of the following: subcutaneous soft tissues, larynx, trachea, oesophagus, recurrent laryngeal nerve
    T4b Tumour invades prevertebral fascia, mediastinal vessels, or encases carotid artery

**Note**
* Including papillary, follicular, poorly differentiated, Hurthle cell and anaplastic carcinomas.

N – Regional Lymph Nodes

NX Regional lymph nodes cannot be assessed

No No regional lymph node metastasis

N1 Regional lymph node metastasis
    N1a Metastasis in Level VI (pretracheal, paratracheal, and prelaryngeal/Delphian lymph nodes) or upper/superior mediastinum
    N1b Metastasis in other unilateral, bilateral or contralateral cervical (Levels I, II III, IV, or V) or retropharyngeal

M – Distant Metastasis

M0 No distant metastasis

M1 Distant metastasis

**pTNM Pathological Classification**
The pT and pN categories correspond to the T and N categories. For pM see page 8.
pN0 Histological examination of a selective neck dissection specimen will ordinarily include 6 or more lymph nodes. If the lymph nodes are negative, but the number ordinarily examined is not met, classify as pN0.

**Histopathological Types**

The four major histopathological types are:

- Papillary carcinoma (including those with follicular foci)
- Follicular carcinoma (including so-called Hürthle cell carcinoma)
- Medullary carcinoma
- Anaplastic

**Stage**

Separate stage groupings are recommended for papillary and follicular (differentiated), medullary, and anaplastic (undifferentiated) carcinomas:

**Papillary and Follicular* under 55 years**

- Stage I  Any T Any N M0
- Stage II Any T Any N M1

**Papillary or Follicular 55 years and older**

- Stage I  T1a,T1b,T2  N0  M0
- Stage II T3  No  M0
- T1,T2,T3  N1  M0
- Stage III T4a  Any N M0
- Stage IVA T4b  Any N M0
- Stage IVB Any T  Any N M1

**Medullary**

- Stage I  T1a, T1b  No  M0
- Stage II T2, T3  No  M0
- Stage III T1, T2, T3  N1a  M0
- Stage IVA T1, T2, T3  N1b  M0
- T4a  Any N M0
- Stage IVB T4b  Any N M0
- Stage IVC Any T  Any N M1
Anaplastic

Stage IVA T1,T2,T3a    No    Mo
Stage IVB T1,T2,T3a    N1    Mo
Stage IVB T3b,T4a,T4b No,N1 Mo
Stage IVC Any T        Any N M1

Note

* Including papillary, follicular, poorly differentiated, and Hurthle cell carcinomas.

Prognostic Factor Grid – Papillary and Follicular Thyroid Carcinoma

Prognostic factors for survival in differentiated thyroid carcinoma of follicular cell derivation

<table>
<thead>
<tr>
<th>Prognostic factors</th>
<th>Tumour related</th>
<th>Host related</th>
<th>Environment related</th>
</tr>
</thead>
<tbody>
<tr>
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<td>Extrathyroid extension (T category)M category Post, treatment thyroglobulin</td>
<td>Age</td>
<td>Residual disease: Ro, 1 or 2</td>
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<tr>
<td>Additional</td>
<td>N category Site of metastases <em>BRAF V600E</em> mutation</td>
<td>Gender</td>
<td>Extent of resection Iodine ablation Endemic goitre</td>
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<tr>
<td>New and promising</td>
<td>Molecular profile</td>
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</table>


Prognostic Factor Grid – Medullary Cancer

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<tr>
<th>Prognostic factors</th>
<th>Tumour related</th>
<th>Host related</th>
<th>Environment related</th>
</tr>
</thead>
<tbody>
<tr>
<td>Essential</td>
<td>Pre. and postoperative calcitonin and CEA</td>
<td>Age</td>
<td>Extent of resection</td>
</tr>
<tr>
<td>Additional</td>
<td>MEN Germline mutation Calcitonin doubling time</td>
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<tr>
<td>New and promising</td>
<td>Molecular profile</td>
<td></td>
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</tr>
</tbody>
</table>

Digestive System Tumours

Introductory Notes

The following sites and types are included:
- Oesophagus and Oesophagogastric Junction
- Stomach
- Small Intestine
- Appendix
- Colon and Rectum
- Anal Canal and Perianal Skin
- Liver cell carcinoma
- Intrahepatic cholangiocarcinoma
- Gallbladder
- Perihilar Bile Duct
- Distal Extrahepatic Bile Duct
- Ampulla of Vater
- Pancreas
- Neuroendocrine Tumours

Each site is described under the following headings:
- Rules for classification with the procedures for assessing T, N, and M categories; additional methods may be used when they enhance the accuracy of appraisal before treatment
- Anatomical sites and subsites where appropriate
- Definition of the regional lymph nodes
- TNM clinical classification
- pTNM pathological classification
- G Histopathological grading where appropriate
- Stage
- Prognostic factors grid

Regional Lymph Nodes
The number of lymph nodes ordinarily included in a lymphadenectomy specimen is noted at each site.

**Oesophagus**

*(ICD-O-3 C15) Including Oesophagogastric Junction (C16.0)*

**Rules for Classification**

The classification applies only to carcinomas and includes adenocarcinomas of the oesophagogastric/gastroesophageal junction. There should be histological confirmation of the disease and division of cases by topographic localization and histological type. A tumour the epicentre of which is within 2 cm of the oesophagogastric junction and also extends into the oesophagus is classified and staged using the oesophageal scheme. Cancers involving the oesophagogastric junction (OGJ) whose epicentre is within the proximal 2 cm of the cardia (Siewert types I/II) are to be staged as oesophageal cancers.

The following are the procedures for assessing T, N, and M categories.

- **T** categories: Physical examination, imaging, endoscopy (including bronchoscopy), and/or surgical exploration
- **N** categories: Physical examination, imaging, and/or surgical exploration
- **M** categories: Physical examination, imaging, and/or surgical exploration

**Anatomical Subsites**

1. Cervical oesophagus (C15.0): this commences at the lower border of the cricoid cartilage and ends at the thoracic inlet (suprasternal notch), approximately 18 cm from the upper incisor teeth.

2. Intrathoracic oesophagus
   - a. The upper thoracic portion (C15.3) extending from the thoracic inlet to the level of the tracheal bifurcation, approximately 24 cm from the upper incisor teeth
   - b. The mid thoracic portion (C15.4) is the proximal half of the oesophagus between the tracheal bifurcation and the oesophagogastric junction. The lower level is approximately 32 cm from the upper incisor teeth
   - c. The lower thoracic portion (C15.5), approximately 8 cm in length (includes abdominal oesophagus), is the distal half of the oesophagus between the tracheal bifurcation and the oesophagogastric junction. The lower level is approximately 40 cm from the upper incisor teeth

3. Oesophagogastric junction (C16.0). Cancers involving the oesophagogastric junction
(OGJ) whose epicentre is within the proximal 2 cm of the cardia (Siewert types I/II) are to be staged as oesophageal cancers. Cancers whose epicentre is more than 2 cm distal from the OGJ will be staged using the Stomach Cancer TNM and Stage even if the OGJ is involved.

**Regional Lymph Nodes**

The regional lymph nodes, irrespective of the site of the primary tumour, are those in the oesophageal drainage area including coeliac axis nodes and paraesophageal nodes in the neck but not the supraclavicular nodes.

**TNM Clinical Classification**

**T – Primary Tumour**

- **TX** Primary tumour cannot be assessed
- **T0** No evidence of primary tumour
- **Tis** Carcinoma in situ/high grade dysplasia
- **T1** Tumour invades lamina propria, muscularis mucosae, or submucosa
  - **T1a** Tumour invades lamina propria or muscularis mucosae
  - **T1b** Tumour invades submucosa
- **T2** Tumour invades muscularis propria
- **T3** Tumour invades adventitia
- **T4** Tumour invades adjacent structures
  - **T4a** Tumour invades pleura, pericardium, azygos vein, diaphragm, or peritoneum
  - **T4b** Tumour invades other adjacent structures such as aorta, vertebral body, or trachea

**N – Regional Lymph Nodes**

- **NX** Regional lymph nodes cannot be assessed
- **N0** No regional lymph node metastasis
- **N1** Metastasis in 1 to 2 regional lymph nodes
- **N2** Metastasis in 3 to 6 regional lymph nodes
- **N3** Metastasis in 7 or more regional lymph nodes

**M – Distant Metastasis**

- **M0** No distant metastasis
- **M1** Distant metastasis
pTNM Pathological Classification
The pT and pN categories correspond to the T and N categories. For pM see page 8.

pN0 Histological examination of a regional lymphadenectomy specimen will ordinarily include 7 or more lymph nodes. If the lymph nodes are negative, but the number ordinarily examined is not met, classify as pN0.

Stage and Prognostic Group – Carcinomas of the Oesophagus and Oesophagogastric Junction*

Squamous Cell Carcinoma

Clinical Stage

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Pathological Stage

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</tr>
<tr>
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<td>T1</td>
<td>N2</td>
<td>Mo</td>
<td>Any</td>
<td>Any</td>
</tr>
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### Adenocarcinoma

#### Clinical Stage

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<th>N</th>
<th>M</th>
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<tbody>
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</tr>
<tr>
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<td>No</td>
<td>Mo</td>
</tr>
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<td>T1</td>
<td>N1</td>
<td>Mo</td>
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<td>Mo</td>
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Stage IVA T1–T4a N2 Mo
  T4b  No, N1, N2 Mo

Any T N3 Mo
Stage IVB Any T Any N M1

Pathological Stage

<table>
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<tr>
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<th>N</th>
<th>M</th>
<th>Grade</th>
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<tbody>
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<td>Mo</td>
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<td>N1, N2 Mo</td>
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<td>T4a</td>
<td>No, N1 Mo</td>
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<td>T4a</td>
<td>N2</td>
<td>Mo</td>
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<tr>
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<td>T4b</td>
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<td>Mo</td>
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Pathological Prognostic Group
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<th>Prognostic factors</th>
<th>Tumour related</th>
<th>Host related</th>
<th>Treatment related</th>
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</thead>
<tbody>
<tr>
<td><strong>Essential</strong></td>
<td>Depth of invasion Lymph node involvement Presence of lymphovascular invasion (LVI)</td>
<td>Performance status Age Nutritional status</td>
<td>Quality of surgery Multimodality approach</td>
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<tr>
<td><strong>Additional</strong></td>
<td>Tumour grading Tumour location</td>
<td>Economic status</td>
<td>Nutritional support</td>
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<tr>
<td><strong>New and promising</strong></td>
<td>CEA, VEGF.C, HER2</td>
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<td></td>
</tr>
</tbody>
</table>


**Note**
- The AJCC publishes prognostic groups for adenocarcinoma and squamous cell carcinoma after neoadjuvant therapy (categories with the prefix “y”).

**Stomach**
(†ICD-O-3 C16)

**Rules for Classification**
The classification applies only to carcinomas. There should be histological confirmation of the disease. Cancers involving the oesophagogastric junction (OGJ) whose epicentre is
within the proximal 2 cm of the cardia (Siewert types I/II) are to be staged as oesophageal cancers. Cancers whose epicentre is more than 2 cm distal from the OGJ will be staged using the Stomach Cancer TNM and Stage even if the OGJ is involved.

Changes in this edition from the seventh edition are based upon recommendations from the International Gastric Cancer Association Staging Project.\(^1\)

The following are the procedures for assessing T, N, and M categories.

**T categories**  
Physical examination, imaging, endoscopy, and/or surgical exploration

**N categories**  
Physical examination, imaging, and/or surgical exploration

**M categories**  
Physical examination, imaging, and/or surgical exploration

### Anatomical Subsites

1. Cardia (16.0)
2. Fundus (C16.1)
3. Corpus (C16.2)
4. Antrum (C16.3) and pylorus (C16.4)

### Regional Lymph Nodes

The regional lymph nodes of the stomach are the perigastric nodes along the lesser and greater curvatures, the nodes along the left gastric, common hepatic, splenic, and coeliac arteries, and the hepatoduodenal nodes.

Involvement of other intra-abdominal lymph nodes such as retropancreatic, mesenteric, and para-aortic is classified as distant metastasis.

### TNM Clinical Classification

#### T – Primary Tumour

**TX** Primary tumour cannot be assessed

**T0** No evidence of primary tumour

**Tis** Carcinoma in situ: intraepithelial tumour without invasion of the lamina propria, high-grade dysplasia

**T1** Tumour invades lamina propria, muscularis mucosae, or submucosa

- **T1a** Tumour invades lamina propria or muscularis mucosae
- **T1b** Tumour invades submucosa

**T2** Tumour invades muscularis propria

**T3** Tumour invades subserosa
T4 Tumour perforates serosa (visceral peritoneum) or invades adjacent structures\textsuperscript{a, b, c}

T4a Tumour perforates serosa

T4b Tumour invades adjacent structures\textsuperscript{a, b}

Notes

\textsuperscript{a} The adjacent structures of the stomach are the spleen, transverse colon, liver, diaphragm, pancreas, abdominal wall, adrenal gland, kidney, small intestine, and retroperitoneum.

\textsuperscript{b} Intramural extension to the duodenum or oesophagus is classified by the depth of greatest invasion in any of these sites including stomach.

\textsuperscript{c} Tumour that extends into gastrocolic or gastrohepatic ligaments or into greater or lesser omentum, without perforation of visceral peritoneum, is T3.

N – Regional Lymph Nodes

- NX Regional lymph nodes cannot be assessed
- N0 No regional lymph node metastasis
- N1 Metastasis in 1 to 2 regional lymph nodes
- N2 Metastasis in 3 to 6 regional lymph nodes
- N3 Metastasis in 7 or more regional lymph nodes
  - N3a Metastasis in 7 to 15 regional lymph nodes
  - N3b Metastasis in 16 or more regional lymph nodes

M – Distant Metastasis

- M0 No distant metastasis
- M1 Distant metastasis

Note

Distant metastasis includes peritoneal seeding, positive peritoneal cytology, and omental tumour not part of continuous extension.

pTNM Pathological Classification

The pT and pN categories correspond to the T and N categories. For pM see page 8.

pN0 Histological examination of a regional lymphadenectomy specimen will ordinarily include 16 or more lymph nodes. If the lymph nodes are negative, but the number
ordinarily examined is not met, classify as pN0.

**Clinical Stage**

<table>
<thead>
<tr>
<th>Stage</th>
<th>T</th>
<th>N</th>
<th>M</th>
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</thead>
<tbody>
<tr>
<td>I</td>
<td>T1, T2</td>
<td>No</td>
<td>Mo</td>
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<tr>
<td>IIA</td>
<td>T1, T2</td>
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<td>Mo</td>
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<td>III</td>
<td>T3, T4a</td>
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<td>Any T</td>
<td>Any N</td>
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**Pathological Stage**

<table>
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<tr>
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<th>N</th>
<th>M</th>
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</thead>
<tbody>
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<td>Tis</td>
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<td>IA</td>
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<td>Mo</td>
</tr>
<tr>
<td>IB</td>
<td>T1</td>
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<td>Mo</td>
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<td>No</td>
<td>Mo</td>
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<td>T1</td>
<td>N2</td>
<td>Mo</td>
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<td>N1</td>
<td>Mo</td>
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<tr>
<td></td>
<td>T3</td>
<td>No</td>
<td>Mo</td>
</tr>
<tr>
<td>IIB</td>
<td>T1</td>
<td>N3a</td>
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<td>N2</td>
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<td>T4a</td>
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<td>Mo</td>
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<td>T3, T4a</td>
<td>N3b</td>
<td>Mo</td>
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<tr>
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<td>T4b</td>
<td>N3a, N3b</td>
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<td>IV</td>
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<td>Any N</td>
<td>M1</td>
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</table>

**Note**

* The AJCC publishes prognostic groups for adenocarcinoma and squamous cell
carcinoma after neoadjuvant therapy (categories with the prefix “y”).

Prognostic Factor Grid – Stomach

Prognostic factors for survival in gastric adenocarcinoma

<table>
<thead>
<tr>
<th>Prognostic factors</th>
<th>Tumour related</th>
<th>Host related</th>
<th>Environment related</th>
</tr>
</thead>
<tbody>
<tr>
<td>Essential</td>
<td>T category N category M category HER2 status</td>
<td></td>
<td>Residual disease: R0, R1 or R2</td>
</tr>
</tbody>
</table>
| Additional             | Tumour site: cardia or distal stomach
                    Histological type Vessel infiltration  | Age                                | Extent of resection |
| New and promising      | Molecular profile                                   | Race: Asian or non Asian           |                     |


Reference


Small Intestine

(ICD-O-3 C17)

Rules for Classification

The classification applies only to carcinomas. There should be histological confirmation of the disease.

The following are the procedures for assessing T, N, and M categories.

- **T categories**  Physical examination, imaging, endoscopy, and/or surgical exploration
- **N categories**  Physical examination, imaging, and/or surgical exploration
- **M categories**  Physical examination, imaging, and/or surgical exploration

Anatomical Subsites

1. Duodenum (C17.0)
2. Jejunum (C17.1)
Note

This classification does not apply to carcinomas of the ampulla of Vater (see page 91).

Regional Lymph Nodes

The regional lymph nodes for the duodenum are the pancreaticoduodenal, pyloric, hepatic (pericholedochal, cystic, hilar), and superior mesenteric nodes.

The regional lymph nodes for the ileum and jejunum are the mesenteric nodes, including the superior mesenteric nodes, and, for the terminal ileum only, the ileocolic nodes including the posterior caecal nodes.

TNM Clinical Classification

T – Primary Tumour

TX Primary tumour cannot be assessed
To No evidence of primary tumour
Tis Carcinoma in situ

T1 Tumour invades lamina propria, muscularis mucosae or submucosa
   T1a Tumour invades lamina propria or muscularis mucosae
   T1b Tumour invades submucosa

T2 Tumour invades muscularis propria

T3 Tumour invades subserosa or non-peritonealized perimuscular tissue (mesentery or retroperitoneum*) without perforation of the serosa

T4 Tumour perforates visceral peritoneum or directly invades other organs or structures (includes other loops of small intestine, mesentery, or retroperitoneum and abdominal wall by way of serosa; for duodenum only, invasion of pancreas)

Note

* The non-peritonealized perimuscular tissue is, for jejunum and ileum, part of the mesentery and, for duodenum in areas where serosa is lacking, part of the retroperitoneum.

N – Regional Lymph Nodes

NX Regional lymph nodes cannot be assessed
No No regional lymph node metastasis
N1 Metastasis in 1 to 2 regional lymph nodes
M – Distant Metastasis

M0 No distant metastasis
M1 Distant metastasis

pTNM Pathological Classification

The pT and pN categories correspond to the T and N categories. For pM see page 8.

pN0 Histological examination of a regional lymphadenectomy specimen will ordinarily include 6 or more lymph nodes. If the lymph nodes are negative, but the number ordinarily examined is not met, classify as pN0.

Stage

Stage 0  Tis  No  Mo
Stage I  T1, T2 No  Mo
Stage IIA  T3  No  Mo
Stage IIB  T4  No  Mo
Stage IIIA Any T N1  Mo
Stage IIIB Any T N2  Mo
Stage IV  Any T Any N M1

Appendix

(ICD-O-3 C18.1)

Rules for Classification

The classification applies to adenocarcinomas of the appendix. Neuroendocrine carcinomas are classified separately (page 97). There should be histological confirmation of the disease and separation of carcinomas into mucinous and non-mucinous adenocarcinomas.

Goblet cell carcinoids are classified according to the carcinoma scheme.

Grading is of particular importance for mucinous tumours.

The following are the procedures for assessing T, N, and M categories.

T categories  Physical examination, imaging, and/or surgical exploration
N categories  Physical examination, imaging, and/or surgical exploration
M categories  Physical examination, imaging, and/or surgical exploration
Anatomical Site
Appendix (C18.1)

Regional Lymph Nodes
The ileocolic are the regional lymph nodes.

TNM Clinical Classification

T – Primary Tumour

TX Primary tumour cannot be assessed
To No evidence of primary tumour
Tis Carcinoma in situ: intraepithelial or invasion of lamina propria a

Tis  Low grade appendiceal mucinous neoplasm confined to the appendix (defined (LAMN) as involvement by acellular mucin or mucinous epithelium that may extend into muscularis propria)
T1  Tumour invades submucosa
T2  Tumour invades muscularis propria
T3  Tumour invades subserosa or mesoappendix
T4  Tumour perforates visceral peritoneum, including mucinous peritoneal tumour or acellular mucin on the serosa of the appendix or mesoappendix and/or directly invades other organs or structures b,c,d
T4a Tumour perforates visceral peritoneum, including mucinous peritoneal tumour or acellular mucin on the serosa of the appendix or mesoappendix
T4b Tumour directly invades other organs or structures

Notes

a Tis includes cancer cells confined within the glandular basement membrane (intraepithelial) or lamina propria (intramucosal) with no extension through muscularis mucosae into submucosa.
b Direct invasion in T4 includes invasion of other intestinal segments by way of the serosa, e.g., invasion of ileum.
c Tumour that is adherent to other organs or structures, macroscopically, is classified cT4b. However, if no tumour is present in the adhesion, microscopically, the classification should be pT1, 2, or 3.
d LAMN with involvement of the subserosa or the serosal surface (visceral peritoneum)
should be classified as T3 or T4a respectively.

**N – Regional Lymph Nodes**

NX Regional lymph nodes cannot be assessed
No No regional lymph node metastasis
N1 Metastasis in 1 to 3 regional lymph nodes
   N1a Metastases in 1 regional lymph node
   N1b Metastases in 2–3 regional lymph nodes
   N1c Tumour deposit(s), i.e. satellites,* in the subserosa, or in non.peritonealized pericolic or perirectal soft tissue *without* regional lymph node metastasis
N2 Metastasis in 4 or more regional lymph nodes

**Note**

* Tumour deposits (satellites) are discrete macroscopic or microscopic nodules of cancer in the pericolo Rectal adipose tissue’s lymph drainage area of a primary carcinoma that are discontinuous from the primary and without histological evidence of residual lymph node or identifiable vascular or neural structures. If a vessel wall is identifiable on H&E, elastic or other stains, it should be classified as venous invasion (V1/2) or lymphatic invasion (L1). Similarly, if neural structures are identifiable, the lesion should be classified as perineural invasion (Pn1).

**M – Distant Metastasis**

Mo No distant metastasis
M1 Distant metastasis
   M1a Intraperitoneal acellular mucin only
   M1b Intraperitoneal metastasis only, including mucinous epithelium
   M1c Non.peritoneal metastasis

**pTNM Pathological Classification**

The pT and pN categories correspond to the T and N categories. For pM see page 8.

pNo Histological examination of a regional lymphadenectomy specimen will ordinarily include 12 or more lymph nodes. If the lymph nodes are negative, but the number ordinarily examined is not met, classify as pNo.

**Stage**

<table>
<thead>
<tr>
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<th>Mo</th>
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</thead>
<tbody>
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</tr>
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<td>M category</td>
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<tr>
<td>---------</td>
<td>------------</td>
<td>------------</td>
<td>------------</td>
</tr>
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</tr>
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<td>Any T</td>
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<td>Mo</td>
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<td>N0</td>
<td>M1a</td>
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<tr>
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<td>Any N</td>
<td>M1b G1</td>
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<tr>
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<td>Any N</td>
<td>M1b G2, G3, GX</td>
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</tbody>
</table>

**Colon and Rectum**  
*(ICD-O-3 C18-20)*

**Rules for Classification**

The classification applies only to carcinomas. There should be histological confirmation of the disease.

The following are the procedures for assessing the T, N, and M categories.

- **T categories**  
  Physical examination, imaging, endoscopy, and/or surgical exploration

- **N categories**  
  Physical examination, imaging, and/or surgical exploration

- **M categories**  
  Physical examination, imaging, and/or surgical exploration

**Anatomical Sites and Subsites**

**Colon (C18)**

1. Caecum (C18.0)
2. Ascending colon (C18.2)
3. Hepatic flexure (C18.3)
4. Transverse colon (C18.4)
5. Splenic flexure (C18.5)
6. Descending colon (C18.6)
7. Sigmoid colon (C18.7)
**Rectosigmoid junction (C19)**

**Rectum (C20)**

**Regional Lymph Nodes**

For each anatomical site or subsite the following are regional lymph nodes:

- **Caecum**: ileocolic, right colic
- **Ascending colon**: ileocolic, right colic, middle colic
- **Hepatic flexure**: right colic, middle colic
- **Transverse colon**: right colic, middle colic, left colic, inferior mesenteric
- **Splenic flexure**: middle colic, left colic, inferior mesenteric
- **Descending colon**: left colic, inferior mesenteric
- **Sigmoid colon**: sigmoid, left colic, superior rectal (haemorrhoidal), inferior mesenteric and rectosigmoid
- **Rectum**: superior, middle, and inferior rectal (haemorrhoidal), inferior mesenteric, internal iliac, mesorectal (paraproctal), lateral sacral, presacral, sacral promontory (Gerota)

Metastasis in nodes other than those listed here is classified as distant metastasis.

**TNM Clinical Classification**

**T – Primary Tumour**

- **TX**: Primary tumour cannot be assessed
- **T0**: No evidence of primary tumour
- **Tis**: Carcinoma in situ: invasion of lamina propria\(^a\)

**T1**: Tumour invades submucosa

**T2**: Tumour invades muscularis propria

**T3**: Tumour invades subserosa or into non.peritonealized pericolic or perirectal tissues

**T4**: Tumour directly invades other organs or structures\(^{b,c,d}\) and/or perforates visceral peritoneum

- **T4a**: Tumour perforates visceral peritoneum
- **T4b**: Tumour directly invades other organs or structures
Notes

a Tis includes cancer cells confined within the mucosal lamina propria (intramucosal) with no extension through the muscularis mucosae into the submucosa.
b Invades through to visceral peritoneum to involve the surface.
c Direct invasion in T4b includes invasion of other organs or segments of the colorectum by way of the serosa, as confirmed on microscopic examination, or for tumours in a retroperitoneal or subperitoneal location, direct invasion of other organs or structures by virtue of extension beyond the muscularis propria.
d Tumour that is adherent to other organs or structures, macroscopically, is classified cT4b. However, if no tumour is present in the adhesion, microscopically, the classification should be pT1-3, depending on the anatomical depth of wall invasion.

N – Regional Lymph Nodes

NX Regional lymph nodes cannot be assessed
No No regional lymph node metastasis
N1 Metastasis in 1 to 3 regional lymph nodes
  N1a Metastasis in 1 regional lymph node
  N1b Metastasis in 2 to 3 regional lymph nodes
  N1c Tumour deposit(s), i.e. satellites,* in the subserosa, or in non-peritonealized pericolic or perirectal soft tissue without regional lymph node metastasis
N2 Metastasis in 4 or more regional lymph nodes
  N2a Metastasis in 4–6 regional lymph nodes
  N2b Metastasis in 7 or more regional lymph nodes

Note

* Tumour deposits (satellites) are discrete macroscopic or microscopic nodules of cancer in the pericolorectal adipose tissue’s lymph drainage area of a primary carcinoma that are discontinuous from the primary and without histological evidence of residual lymph node or identifiable vascular or neural structures. If a vessel wall is identifiable on H&E, elastic or other stains, it should be classified as venous invasion (V1/2) or lymphatic invasion (L1). Similarly, if neural structures are identifiable, the lesion should be classified as perineural invasion (Pn1). The presence of tumour deposits does not change the primary tumour T category, but changes the node status (N) to pN1c if all regional lymph nodes are negative on pathological examination.

M – Distant Metastasis
M0 No distant metastasis
M1 Distant metastasis
  M1a Metastasis confined to one organ (liver, lung, ovary, non-regional lymph node(s)) without peritoneal metastases
  M1b Metastasis in more than one organ
  M1c Metastasis to the peritoneum with or without other organ involvement

**TNM Pathological Classification**

The pT and pN categories correspond to the T and N categories. For pM see page 8.

pN0 Histological examination of a regional lymphadenectomy specimen will ordinarily include 12 or more lymph nodes. If the lymph nodes are negative, but the number ordinarily examined is not met, classify as pN0.

**Stage**

<table>
<thead>
<tr>
<th>Stage</th>
<th>T</th>
<th>N</th>
<th>M</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage 0</td>
<td>Tis</td>
<td>No</td>
<td>Mo</td>
</tr>
<tr>
<td>Stage I</td>
<td>T1, T2</td>
<td>No</td>
<td>Mo</td>
</tr>
<tr>
<td>Stage II</td>
<td>T3, T4</td>
<td>No</td>
<td>Mo</td>
</tr>
<tr>
<td>Stage IIA</td>
<td>T3</td>
<td>No</td>
<td>Mo</td>
</tr>
<tr>
<td>Stage IIB</td>
<td>T4a</td>
<td>No</td>
<td>Mo</td>
</tr>
<tr>
<td>Stage IIC</td>
<td>T4b</td>
<td>No</td>
<td>Mo</td>
</tr>
<tr>
<td>Stage III</td>
<td>Any T</td>
<td>N1, N2</td>
<td>Mo</td>
</tr>
<tr>
<td>Stage IIIA</td>
<td>T1, T2</td>
<td>N1</td>
<td>Mo</td>
</tr>
<tr>
<td></td>
<td>T1</td>
<td>N2a</td>
<td>Mo</td>
</tr>
<tr>
<td>Stage IIIB</td>
<td>T1, T2</td>
<td>N2b</td>
<td>Mo</td>
</tr>
<tr>
<td></td>
<td>T2, T3</td>
<td>N2a</td>
<td>Mo</td>
</tr>
<tr>
<td></td>
<td>T3, T4a</td>
<td>N1</td>
<td>Mo</td>
</tr>
<tr>
<td>Stage IIIC</td>
<td>T3, T4a</td>
<td>N2b</td>
<td>Mo</td>
</tr>
<tr>
<td></td>
<td>T4a</td>
<td>N2a</td>
<td>Mo</td>
</tr>
<tr>
<td></td>
<td>T4b</td>
<td>N1, N2</td>
<td>Mo</td>
</tr>
<tr>
<td>Stage IV</td>
<td>Any T</td>
<td>Any N</td>
<td>M1</td>
</tr>
<tr>
<td>Stage IVA</td>
<td>Any T</td>
<td>Any N</td>
<td>M1a</td>
</tr>
<tr>
<td>Stage IVB</td>
<td>Any T</td>
<td>Any N</td>
<td>M1b</td>
</tr>
<tr>
<td>Stage IVC</td>
<td>Any T</td>
<td>Any N</td>
<td>M1c</td>
</tr>
</tbody>
</table>

**Prognostic Factors Grid – Colon and Rectum**
## Prognostic factors for survival in differentiated colorectal cancer

<table>
<thead>
<tr>
<th>Prognostic factors</th>
<th>Tumour related</th>
<th>Host related</th>
<th>Environment related</th>
</tr>
</thead>
<tbody>
<tr>
<td>Essential</td>
<td>T category</td>
<td>Age</td>
<td>Screening programme</td>
</tr>
<tr>
<td></td>
<td>N category</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>M category</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Circumferential margin (rectal cancer)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Additional</td>
<td>Vascular/lymphatic invasion</td>
<td>Race</td>
<td>Socioeconomic status</td>
</tr>
<tr>
<td></td>
<td>Perineural invasion</td>
<td></td>
<td>Centre volume and experience</td>
</tr>
<tr>
<td></td>
<td>Grade Tumour budding</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Perforation</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>KRAS MSI BRAF</td>
<td></td>
<td></td>
</tr>
<tr>
<td>New and promising</td>
<td>Molecular profile</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>


## Anal Canal and Perianal Skin

(ICD-O-3 C21, ICD-O-3 C44.5)

The anal canal extends from rectum to perianal skin (to the junction with hair-bearing skin). It is lined by the mucous membrane overlying the internal sphincter, including the transitional epithelium and dentate line. Tumours of anal margin and perianal skin defined as within 5 cm of the anal margin (ICD.O C44.5) are now classified with carcinomas of the anal canal.

### Rules for Classification

The classification applies only to carcinomas. There should be histological confirmation of the disease and division of cases by histological type.

The following are the procedures for assessing T, N, and M categories.

- **T categories**  Physical examination, imaging, endoscopy, and/or surgical exploration
- **N categories**  Physical examination, imaging, and/or surgical exploration
- **M categories**  Physical examination, imaging, and/or surgical exploration

### Regional Lymph Nodes

The regional lymph nodes are the perirectal, the internal iliac, external iliac, and the inguinal lymph nodes.

### TNM Clinical Classification
T – Primary Tumour
TX Primary tumour cannot be assessed
T0 No evidence of primary tumour
Tis Carcinoma in situ, Bowen disease, high grade squamous intraepithelial lesion (HSIL), anal intraepithelial neoplasia II–III (AIN II–III)

T1 Tumour 2 cm or less in greatest dimension
T2 Tumour more than 2 cm but not more than 5 cm in greatest dimension
T3 Tumour more than 5 cm in greatest dimension
T4 Tumour of any size invades adjacent organ(s), e.g., vagina, urethra, bladder

Note
* Direct invasion of the rectal wall, perianal skin, subcutaneous tissue, or the sphincter muscle(s) alone is not classified as T4.

N – Regional Lymph Nodes
NX Regional lymph nodes cannot be assessed
N0 No regional lymph node metastasis
N1 Metastasis in regional lymph node(s)
    N1a Metastases in inguinal, mesorectal, and/or internal iliac nodes
    N1b Metastases in external iliac nodes
    N1c Metastases in external iliac and in inguinal, mesorectal and/or internal iliac nodes

M – Distant Metastasis
    M0 No distant metastasis
    M1 Distant metastasis

pTNM Pathological Classification
The pT and pN categories correspond to the T and N categories. For pM see page 8.
pNo Histological examination of a regional perirectal/pelvic lymphadenectomy specimen will ordinarily include 12 or more lymph nodes; histological examination of an inguinal lymphadenectomy specimen will ordinarily include 6 or more lymph nodes. If the lymph nodes are negative, but the number ordinarily examined is not met, classify as pNo.

Stage
Stage 0  Tis  No  Mo
Stage I   T1   No  Mo
Stage IIA  T2   No  Mo
Stage IIB  T3   No  Mo
Stage IIIA T1, T2, N1  Mo
Stage IIB  T4   No  Mo
Stage IIIC T3, T4  N1  Mo
Stage IV   Any T  Any N M1

Prognostic Factors Grid – Anal Canal

Prognostic factors for outcome in anal cancer

<table>
<thead>
<tr>
<th>Prognostic factors</th>
<th>Tumour related</th>
<th>Host related</th>
<th>Environment related</th>
</tr>
</thead>
<tbody>
<tr>
<td>Essential</td>
<td>T, N and M category</td>
<td>Age</td>
<td>Cigarette smoking</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Male gender</td>
<td>Social deprivation</td>
</tr>
<tr>
<td>Additional</td>
<td>Skin ulceration</td>
<td>Immune suppression</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Sphincter involvement</td>
<td>Primary tumour size &gt;5 cm</td>
<td>Long term corticosteroids</td>
</tr>
<tr>
<td>New and promising</td>
<td>Squamous cell</td>
<td>Concomitant herpes</td>
<td></td>
</tr>
<tr>
<td></td>
<td>carcinoma antigen (SCCAg)</td>
<td>simplex virus (HSV)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Haemoglobin level</td>
<td></td>
</tr>
</tbody>
</table>


Liver

(ICD-O-3 C 22.0)

Rules for Classification

The classification applies to hepatocellular carcinoma.

Cholangio, (intrahepatic bile duct) carcinoma of the liver has a separate classification (see page 83). There should be histological confirmation of the disease.

The following are the procedures for assessing T, N, and M categories.

T categories  Physical examination, imaging, and/or surgical exploration
N categories  Physical examination, imaging, and/or surgical exploration

M categories  Physical examination, imaging, and/or surgical exploration

**Note**

Although the presence of cirrhosis is an important prognostic factor it does not affect the TNM classification, being an independent prognostic variable.

**Regional Lymph Nodes**

The regional lymph nodes are the hilar, hepatic (along the proper hepatic artery), periportal (along the portal vein), inferior phrenic, and caval nodes.

**TNM Clinical Classification**

**T – Primary Tumour**

<table>
<thead>
<tr>
<th>Category</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>TX</td>
<td>Primary tumour cannot be assessed</td>
</tr>
<tr>
<td>T0</td>
<td>No evidence of primary tumour</td>
</tr>
<tr>
<td>T1a</td>
<td>Solitary tumour 2 cm or less in greatest dimension with or without vascular invasion</td>
</tr>
<tr>
<td>T1b</td>
<td>Solitary tumour more than 2 cm in greatest dimension without vascular invasion</td>
</tr>
<tr>
<td>T2</td>
<td>Solitary tumour with vascular invasion more than 2 cm dimension or multiple tumours, none more than 5 cm in greatest dimension</td>
</tr>
<tr>
<td>T3</td>
<td>Multiple tumours any more than 5 cm in greatest dimension</td>
</tr>
<tr>
<td>T4</td>
<td>Tumour(s) involving a major branch of the portal or hepatic vein with direct invasion of adjacent organs (including the diaphragm), other than the gallbladder or with perforation of visceral peritoneum</td>
</tr>
</tbody>
</table>

**N – Regional Lymph Nodes**

<table>
<thead>
<tr>
<th>Category</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>NX</td>
<td>Regional lymph nodes cannot be assessed</td>
</tr>
<tr>
<td>N0</td>
<td>No regional lymph node metastasis</td>
</tr>
<tr>
<td>N1</td>
<td>Regional lymph node metastasis</td>
</tr>
</tbody>
</table>

**M – Distant Metastasis**

<table>
<thead>
<tr>
<th>Category</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>M0</td>
<td>No distant metastasis</td>
</tr>
<tr>
<td>M1</td>
<td>Distant metastasis</td>
</tr>
</tbody>
</table>

**pTNM Pathological Classification**

The pT and pN categories correspond to the T and N categories. For pM see page 8.
Histological examination of a regional lymphadenectomy specimen will ordinarily include 3 or more lymph nodes. If the lymph nodes are negative, but the number ordinarily examined is not met, classify as pNo.

**Stage – Liver**

- Stage IA  T1a  No  Mo
- Stage IB  T1b  No  Mo
- Stage II  T2  No  Mo
- Stage IIIA T3  No  Mo
- Stage IIIB T4  No  Mo
- Stage IVA Any T N1  Mo
- Stage IVB Any T Any N M1

**Prognostic Factors Grid – Liver**
## Prognostic factors for liver cancer (HCC)

<table>
<thead>
<tr>
<th>Prognostic factors</th>
<th>Tumour related</th>
<th>Host related</th>
<th>Environment related</th>
</tr>
</thead>
</table>
| **Essential**      | Major vascular invasion*  
                    | Microvascular invasion*  
                    | Size >5 cm  
                    | Multiple (vs single)  
                    | Tumour differentiation | Fibrosis of underlying liver*  
                    | Tumour growth rate  
                    | Patient performance status at diagnosis  
                    | Liver function  
                    | Degree of portal hypertension | *Treatment factors*:  
                    | Post-resection residual disease (R0, R1, R2)  
                    | Post-ablation residual disease  
                    | Post-embolization residual disease |
| **Additional**     | AFP level  
                    | DCP/PIVKA.II level | Hepatitis activity |
| **New and promising** | 5-gene score (genetic profile)  
                    | Cancer stem cell markers  
                    | Circulating micro RNA, DNA, circulating cancer cells | IGF.1 combined with CLIP  
                    | Regulatory T cells C, reactive protein (CRP), interleukin 10 (IL.10), vascular endothelial growth factor (VEGF), neutrophil to lymphocyte ratio, Mn SOD (magnesium superoxide dismutase) |

* Dominant prognostic factors in resected/transplanted patients.


## Intrahepatic Bile Ducts

(ICD-O-3 C22.1)

### Rules for Classification

The staging system applies to intrahepatic cholangiocarcinoma, cholangiocellular carcinoma, and combined hepatocellular and cholangiocarcinoma (mixed hepatocellular/cholangiocellular carcinoma).

The following are the procedures for assessing T, N, and M categories.

- **T categories**: Physical examination, imaging, and/or surgical exploration
- **N categories**: Physical examination, imaging, and/or surgical exploration
- **M categories**: Physical examination, imaging, and/or surgical exploration
Regional Lymph Nodes

For right liver intrahepatic cholangiocarcinoma, the regional lymph nodes include the hilar (common bile duct, hepatic artery, portal vein, and cystic duct), periduodenal, and peripancreatic lymph nodes.

For left liver intrahepatic cholangiocarcinoma, regional lymph nodes include hilar and gastrohepatic lymph nodes.

For intrahepatic cholangiocarcinoma, spread to the coeliac and/or periaortic and caval lymph nodes are distant metastases (M1).

**TNM Clinical Classification**

**T – Primary Tumour**

- **TX** Primary tumour cannot be assessed
- **T0** No evidence of primary tumour
- **Tis** Carcinoma in situ (intraductal tumour)
- **T1a** Solitary tumour 5 cm or less in greatest dimension without vascular invasion
- **T1b** Solitary tumour more than 5 cm in greatest dimension without vascular invasion
- **T2** Solitary tumour with intrahepatic vascular invasion or multiple tumours, with or without vascular invasion
- **T3** Tumour perforating the visceral peritoneum
- **T4** Tumour involving local extrahepatic structures by direct hepatic invasion

**N – Regional Lymph Nodes**

- **NX** Regional lymph nodes cannot be assessed
- **N0** No regional lymph node metastasis
- **N1** Regional lymph node metastasis

**M – Distant Metastasis**

- **M0** No distant metastasis
- **M1** Distant metastasis

**pTNM Pathological Classification**

The pT and pN categories correspond to the T and N categories. For pM see page 8.

**pN0** Histological examination of a regional lymphadenectomy specimen will ordinarily include 6 or more lymph nodes. If the regional lymph nodes are negative, but the number ordinarily examined is not met, classify as pN0.
Stage – Intrahepatic Bile Ducts

<table>
<thead>
<tr>
<th>Stage</th>
<th>T</th>
<th>N</th>
<th>M</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>T1</td>
<td>No</td>
<td>Mo</td>
</tr>
<tr>
<td>IA</td>
<td>T1a</td>
<td>No</td>
<td>Mo</td>
</tr>
<tr>
<td>IB</td>
<td>T1b</td>
<td>No</td>
<td>Mo</td>
</tr>
<tr>
<td>II</td>
<td>T2</td>
<td>No</td>
<td>Mo</td>
</tr>
<tr>
<td>IIIA</td>
<td>T3</td>
<td>No</td>
<td>Mo</td>
</tr>
<tr>
<td>IIIB</td>
<td>T4</td>
<td>No</td>
<td>Mo</td>
</tr>
<tr>
<td></td>
<td>Any T</td>
<td>N1</td>
<td>Mo</td>
</tr>
<tr>
<td>IV</td>
<td>Any T</td>
<td>Any N</td>
<td>M1</td>
</tr>
</tbody>
</table>

Gallbladder
(ICD-O-3 C23.0 and C24.0)

Rules for Classification

The classification applies only to carcinomas of gallbladder (C23.0) and cystic duct (C24.0). There should be histological confirmation of the disease.

The following are the procedures for assessing T, N, and M categories.

- **T categories**  Physical examination, imaging, and/or surgical exploration
- **N categories**  Physical examination, imaging, and/or surgical exploration
- **M categories**  Physical examination, imaging, and/or surgical exploration

Regional Lymph Nodes

Regional lymph nodes are the hepatic hilus nodes (including nodes along the common bile duct, hepatic artery, portal vein, and cystic duct), coeliac, and superior mesenteric artery nodes.

TNM Clinical Classification

**T – Primary Tumour**

- **TX** Primary tumour cannot be assessed
- **To** No evidence of primary tumour
- **Tis** Carcinoma in situ
- **T1** Tumour invades lamina propria or muscular layer
  - **T1a** Tumour invades lamina propria
  - **T1b** Tumour invades muscular layer
T2 Tumour invades perimuscular connective tissue; no extension beyond serosa or into liver

T2a Tumour invades perimuscular connective tissue on the peritoneal side with no extension to the serosa

T2b Tumour invades perimuscular connective tissue on the hepatic side with no extension into the liver

T3 Tumour perforates the serosa (visceral peritoneum) and/or directly invades the liver and/or one other adjacent organ or structure, such as stomach, duodenum, colon, pancreas, omentum, extrahepatic bile ducts

T4 Tumour invades main portal vein or hepatic artery or invades two or more extrahepatic organs or structures

**N – Regional Lymph Nodes**

<table>
<thead>
<tr>
<th></th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>NX</td>
<td>Regional lymph nodes cannot be assessed</td>
</tr>
<tr>
<td>N0</td>
<td>No regional lymph node metastasis</td>
</tr>
<tr>
<td>N1</td>
<td>Metastases to 1–3 regional nodes</td>
</tr>
<tr>
<td>N2</td>
<td>Metastasis to 4 or more regional nodes</td>
</tr>
</tbody>
</table>

**M – Distant Metastasis**

<table>
<thead>
<tr>
<th></th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mo</td>
<td>No distant metastasis</td>
</tr>
<tr>
<td>M1</td>
<td>Distant metastasis</td>
</tr>
</tbody>
</table>

**pTNM Pathological Classification**

The pT and pN categories correspond to the T and N categories. For pM see page 8.

pNo Histological examination of a regional lymphadenectomy specimen will ordinarily include 6 or more lymph nodes. If the regional lymph nodes are negative, but the number ordinarily examined is not met, classify as pNo.

**Stage – Gallbladder**

<table>
<thead>
<tr>
<th>Stage</th>
<th>T Category</th>
<th>N Category</th>
<th>M Category</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage 0</td>
<td>Tis</td>
<td>No</td>
<td>Mo</td>
</tr>
<tr>
<td>Stage IA</td>
<td>T1a</td>
<td>No</td>
<td>Mo</td>
</tr>
<tr>
<td>Stage IB</td>
<td>T1b</td>
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<td>Mo</td>
</tr>
<tr>
<td>Stage IIA</td>
<td>T2a</td>
<td>No</td>
<td>Mo</td>
</tr>
<tr>
<td>Stage IIB</td>
<td>T2b</td>
<td>No</td>
<td>Mo</td>
</tr>
<tr>
<td>Stage IIIA</td>
<td>T3</td>
<td>No</td>
<td>Mo</td>
</tr>
<tr>
<td>Stage IIIB</td>
<td>T1, T2, T3 N1</td>
<td>No</td>
<td>Mo</td>
</tr>
</tbody>
</table>
Stage IVA  T4  No, N1 Mo
Stage IVB  Any T  N2  Mo
           Any T  Any N  M1

Perihilar Bile Ducts
(ICD-O-3 C24.0)

Rules for Classification
The classification applies to carcinomas of the extrahepatic bile ducts of perihilar localization (Klatskin tumour). Included are the right, left and the common hepatic ducts. The following are the procedures for assessing T, N, and M categories.

T categories  Physical examination, imaging, and/or surgical exploration
N categories  Physical examination, imaging, and/or surgical exploration
M categories  Physical examination, imaging, and/or surgical exploration

Anatomical Sites and Subsites
Perihilar cholangiocarcinomas are tumours located in the extrahepatic biliary tree proximal to the origin of the cystic duct.

Regional Lymph Nodes
The regional nodes are the hilar and pericholedochal nodes in the hepatoduodenal ligament.

TNM Clinical Classification

T – Primary Tumour

TX  Primary tumour cannot be assessed
To  No evidence of primary tumour
Tis  Carcinoma in situ

T1  Tumour confined to the bile duct, with extension up to the muscle layer or fibrous tissue
T2a Tumour invades beyond the wall of the bile duct to surrounding adipose tissue
T2b Tumour invades adjacent hepatic parenchyma
T3  Tumour invades unilateral branches of the portal vein or hepatic artery
T4  Tumour invades the main portal vein or its branches bilaterally; or the common
hepatic artery; or unilateral second order biliary radicals with contralateral portal vein or hepatic artery involvement

**N – Regional Lymph Nodes**

NX Regional lymph nodes cannot be assessed  
No No regional lymph node metastasis  
N1 Metastases to 1–3 regional lymph nodes  
N2 Metastases to 4 or more regional nodes

**M – Distant Metastasis**

M0 No distant metastasis  
M1 Distant metastasis

**pTNM Pathological Classification**

The pT and pN categories correspond to the T and N categories. For pM see page 8.

pNo Histological examination of a regional lymphadenectomy specimen will ordinarily include 15 more lymph nodes. If the regional lymph nodes are negative, but the number ordinarily examined is not met, classify as pNo.

**Stage – Perihilar Bile Ducts**

<table>
<thead>
<tr>
<th>Stage</th>
<th>T</th>
<th>N</th>
<th>M</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Tis</td>
<td>No</td>
<td>Mo</td>
</tr>
<tr>
<td>I</td>
<td>T1</td>
<td>No</td>
<td>Mo</td>
</tr>
<tr>
<td>II</td>
<td>T2a, T2b</td>
<td>No</td>
<td>Mo</td>
</tr>
<tr>
<td>IIIA</td>
<td>T3</td>
<td>No</td>
<td>Mo</td>
</tr>
<tr>
<td>IIIB</td>
<td>T4</td>
<td>No</td>
<td>Mo</td>
</tr>
<tr>
<td>IIIC</td>
<td>Any T</td>
<td>N1</td>
<td>Mo</td>
</tr>
<tr>
<td>IVA</td>
<td>Any T</td>
<td>N2</td>
<td>Mo</td>
</tr>
<tr>
<td>IVB</td>
<td>Any T</td>
<td>Any N</td>
<td>M1</td>
</tr>
</tbody>
</table>

**Distal Extrahepatic Bile Duct**

*ICD-O-3 C24.0*

**Rules for Classification**

The classification applies to carcinomas of the extrahepatic bile ducts distal to the insertion of the cystic duct. Cystic duct carcinoma is included under gallbladder.
The following are the procedures for assessing T, N, and M categories.

   T categories  Physical examination, imaging, and/or surgical exploration
   N categories  Physical examination, imaging, and/or surgical exploration
   M categories  Physical examination, imaging, and/or surgical exploration

Regional Lymph Nodes

The regional lymph nodes are along the common bile duct, hepatic artery, back towards the coeliac trunk, posterior and anterior pancreaticoduodenal nodes, and nodes along the superior mesenteric artery.

TNM Clinical Classification

T – Primary Tumour

   TX  Primary tumour cannot be assessed
   T0  No evidence of primary tumour
   Tis Carcinoma in situ

T1  Tumour invades bile duct wall to a depth less than 5 mm
T2  Tumour invades bile duct wall to a depth of 5 mm up to 12 mm
T3  Tumour invades bile duct wall to a depth of more than 12 mm
T4  Tumour involves the coeliac axis, the superior mesenteric artery and/or the common hepatic artery

N – Regional Lymph Nodes

   NX  Regional lymph nodes cannot be assessed
   N1  Metastases to 1–3 regional nodes
   N2  Metastasis to 4 or more regional nodes

M – Distant Metastasis

   MO  No distant metastasis
   M1  Distant metastasis

pTNM Pathological Classification

The pT and pN categories correspond to the T and N categories. For pM see page 8.

pNo  Histological examination of a regional lymphadenectomy specimen will ordinarily include 12 or more lymph nodes. If the regional lymph nodes are negative, but the number ordinarily examined is not met, classify as pNo.
Stage – Distal Extrahepatic Bile Duct

<table>
<thead>
<tr>
<th>Stage</th>
<th>Tumour</th>
<th>Node</th>
<th>Metastatic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage 0</td>
<td>Tis</td>
<td>No</td>
<td>Mo</td>
</tr>
<tr>
<td>Stage I</td>
<td>T1</td>
<td>No</td>
<td>Mo</td>
</tr>
<tr>
<td>Stage IIA</td>
<td>T1, T2</td>
<td>N1</td>
<td>Mo</td>
</tr>
<tr>
<td></td>
<td></td>
<td>N0</td>
<td>Mo</td>
</tr>
<tr>
<td>Stage IIB</td>
<td>T2, T3</td>
<td>N1</td>
<td>Mo, N1 Mo</td>
</tr>
<tr>
<td>Stage IIIA</td>
<td>T1, T2, T3</td>
<td>N2</td>
<td>Mo</td>
</tr>
<tr>
<td>Stage IIIB</td>
<td>T4</td>
<td>Any N</td>
<td>Mo</td>
</tr>
<tr>
<td>Stage IV</td>
<td>Any T</td>
<td>Any N</td>
<td>M1</td>
</tr>
</tbody>
</table>

Prognostic Factor Grid – Biliary Tract and Gallbladder Cancers

Prognostic risk factors in biliary tract carcinoma

<table>
<thead>
<tr>
<th>Prognostic factors</th>
<th>Tumour related</th>
<th>Host related</th>
<th>Environment related</th>
</tr>
</thead>
<tbody>
<tr>
<td>Essential</td>
<td>Resectable</td>
<td>ECOG status</td>
<td>Residual disease (R0, R1, R2)</td>
</tr>
<tr>
<td>Additional</td>
<td>Lymph node metastases</td>
<td></td>
<td></td>
</tr>
<tr>
<td>New and promising</td>
<td>FGFR2 mutations</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>


Ampulla of Vater

(ICD-O C24.1)

Rules for Classification

The classification applies only to carcinomas. There should be histological confirmation of the disease.

The following are the procedures for assessing T, N, and M categories.

- **T categories**: Physical examination, imaging, and/or surgical exploration
- **N categories**: Physical examination, imaging, and/or surgical exploration
- **M categories**: Physical examination, imaging, and/or surgical exploration
Regional Lymph Nodes

The regional lymph nodes are the same as for the head of the pancreas and are the lymph nodes along the common bile duct, common hepatic artery, portal vein, pyloric, infrapyloric, subpyloric, proximal mesenteric, coeliac, posterior and anterior pancreaticoduodenal vessels, and along the superior mesenteric vein and right lateral wall of the superior mesenteric artery.

Note

The splenic lymph nodes and those of the tail of the pancreas are not regional; metastases to these lymph nodes are coded M1.

TNM Clinical Classification

T – Primary Tumour

TX Primary tumour cannot be assessed
To No evidence of primary tumour
Tis Carcinoma in situ

T1a Tumour limited to ampulla of Vater or sphincter of Oddi
T1b Tumour invades beyond the sphincter of Oddi (perisphincteric invasion) and/or into the duodenal submucosa
T2 Tumour invades the muscularis propria of the duodenum
T3 Tumour invades pancreas
  T3a Tumour invades 0.5 cm or less into the pancreas
  T3b Tumour invades more than 0.5 cm into the pancreas or extends into peripancreatic tissue or duodenal serosa but without involvement of the celiac axis or the superior mesenteric artery
T4 Tumour with vascular involvement of the superior mesenteric artery or celiac axis, or common hepatic artery

N – Regional Lymph Nodes

NX Regional lymph nodes cannot be assessed
No No regional lymph node metastasis
N1 Metastasis in 1 or 2 regional lymph nodes
N2 Metastasis in 3 or more regional lymph nodes

M – Distant Metastasis

Mo No distant metastasis
**pTNM Pathological Classification**

The pT and pN categories correspond to the T and N categories. For pM see page 8.

pN0 Histological examination of a regional lymphadenectomy specimen will ordinarily include 12 or more lymph nodes. If the lymph nodes are negative, but the number ordinarily examined is not met, classify as pN0.

### Stage – Ampulla of Vater

<table>
<thead>
<tr>
<th>Stage</th>
<th>T</th>
<th>N</th>
<th>M</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage 0</td>
<td>Tis</td>
<td>No</td>
<td>Mo</td>
</tr>
<tr>
<td>Stage IA</td>
<td>T1a</td>
<td>No</td>
<td>Mo</td>
</tr>
<tr>
<td>Stage IB</td>
<td>T1b, T2</td>
<td>No</td>
<td>Mo</td>
</tr>
<tr>
<td>Stage IIA</td>
<td>T3a</td>
<td>No</td>
<td>Mo</td>
</tr>
<tr>
<td>Stage IIB</td>
<td>T3b</td>
<td>No</td>
<td>Mo</td>
</tr>
<tr>
<td>Stage IIIA</td>
<td>T1a, T1b, T2, T3</td>
<td>N1</td>
<td>Mo</td>
</tr>
<tr>
<td>Stage IIIB</td>
<td>Any T</td>
<td>N2</td>
<td>Mo</td>
</tr>
<tr>
<td>Stage IIIB</td>
<td>T4</td>
<td>Any N</td>
<td>Mo</td>
</tr>
<tr>
<td>Stage IV</td>
<td>Any T</td>
<td>Any N</td>
<td>M1</td>
</tr>
</tbody>
</table>

### Pancreas

(ICD-O-3 C25)

#### Rules for Classification

The classification applies to carcinomas of the exocrine pancreas and/or high grade neuroendocrine carcinomas. Well differentiated neuroendocrine tumours of the pancreas are classified as shown on page 102. There should be histological or cytological confirmation of the disease.

The following are the procedures for assessing T, N, and M categories.

- **T categories** Physical examination, imaging, and/or surgical exploration
- **N categories** Physical examination, imaging, and/or surgical exploration
- **M categories** Physical examination, imaging, and/or surgical exploration

### Anatomical Subsites

C25.0 Head of pancreas
C25.1 Body of pancreas
Notes

a Tumours of the head of the pancreas are those arising to the right of the left border of the superior mesenteric vein. The uncinate process is considered as part of the head.

b Tumours of the body are those arising between the left border of the superior mesenteric vein and left border of the aorta.

c Tumours of the tail are those arising between the left border of the aorta and the hilum of the spleen.

Regional Lymph Nodes

The regional lymph nodes for tumours in the head and neck of the pancreas are the lymph nodes along the common bile duct, common hepatic artery, portal vein, pyloric, infrapyloric, subpyloric, proximal mesenteric, coeliac, posterior, and anterior pancreaticoduodenal vessels, and along the superior mesenteric vein and right lateral wall of the superior mesenteric artery.

The regional lymph nodes for tumours in body and tail are the lymph nodes along the common hepatic artery, coeliac axis, splenic artery, and splenic hilum, as well as retroperitoneal nodes and lateral aortic nodes.

TNM Clinical Classification

T – Primary Tumour

TX Primary tumour cannot be assessed
To No evidence of primary tumour
Tis Carcinoma in situ*

T1 Tumour 2 cm or less in greatest dimension
   T1a Tumour 0.5 cm or less in greatest dimension
   T1b Tumour greater than 0.5 cm and less than 1 cm in greatest dimension
   T1c Tumour greater than 1 cm but no more than 2 cm in greatest dimension

T2 Tumour more than 2 cm but no more than 4 cm in greatest dimension

T3 Tumour and more than 4 cm in greatest dimension

T4 Tumour involves coeliac axis, superior mesenteric artery and/or common hepatic artery
Note

* Tis also includes the ‘PanIN–III’ classification.

N – Regional Lymph Nodes

NX Regional lymph nodes cannot be assessed
N0 No regional lymph node metastasis
N1 Metastases in 1 to 3 regional lymph node
N2 Metastases in 4 or more regional lymph node

M – Distant Metastasis

M0 No distant metastasis
M1 Distant metastasis

pTNM Pathological Classification

The pT and pN categories correspond to the T and N categories. For pM see page 8.

pN0 Histological examination of a regional lymphadenectomy specimen will ordinarily include 12 or more lymph nodes. If the lymph nodes are negative, but the number ordinarily examined is not met, classify as pN0.

Stage – Pancreas

Stage 0 Tis No Mo
Stage IA T1 No Mo
Stage IB T2 No Mo
Stage IIA T3 No Mo
Stage IIB T1, T2, T3 N1 Mo
Stage III T1, T2, T3 N2 Mo
Stage IV Any T Any N M1

Prognostic Factors Grid – Pancreas
Well-Differentiated Neuroendocrine Tumours of the Gastrointestinal Tract

Rules for Classification

This classification system applies to well differentiated neuroendocrine tumours (carcinoid tumours and atypical carcinoid tumours) of the gastrointestinal tract, including the pancreas. Neuroendocrine tumours of the lung should be classified according to criteria for carcinoma of the lung. Merkel cell carcinoma of the skin has a separate classification.

High grade (Grade 3) neuroendocrine carcinomas are excluded and should be classified according to criteria for classifying carcinomas at the respective site.

Histopathological Grading

The following grading scheme has been proposed for all gastrointestinal neuroendocrine tumours:

<table>
<thead>
<tr>
<th>Grade</th>
<th>Mitotic count (per 10 HPF)</th>
<th>Ki.67 index (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>G1</td>
<td>&lt;2</td>
<td>≤2</td>
</tr>
<tr>
<td>G2</td>
<td>2–20</td>
<td>3–20</td>
</tr>
<tr>
<td>G3</td>
<td>&gt;20</td>
<td>&gt;20</td>
</tr>
</tbody>
</table>

Notes
a 10 HPF (high power fields) = 2 mm²; at least 40 fields (at 40× magnification) evaluated in areas of highest mitotic density.

b MIB1 antibody; % of 500–2000 tumour cells in areas of highest nuclear labelling.

**Well-Differentiated Neuroendocrine Tumours (G1 and G2) – Gastric, Jejunum/Ileum, Appendix, Colonic, and Rectal**

**Regional lymph nodes**
The regional lymph nodes correspond to those listed under the appropriate sites for carcinoma.

**TNM Clinical Classification**

**Stomach**

**T – Primary Tumour**

T\(\text{ X}\) Primary tumour cannot be assessed
T\(\text{ 0}\) No evidence of primary tumour
T1 Tumour invades lamina propria or submucosa and 1 cm or less in greatest dimension
T2 Tumour invades muscularis propria or is more than 1 cm in greatest dimension
T3 Tumour invades subserosa
T4 Tumour perforates visceral peritoneum (serosa) or invades other organs or adjacent structures

**Note**
For any T, add (m) for multiple tumours.

**N – Regional Lymph Nodes**

N\(\text{ X}\) Regional lymph nodes cannot be assessed
N\(\text{ 0}\) No regional lymph node metastasis
N\(\text{ 1}\) Regional lymph node metastasis

**M – Distant Metastasis**

M\(\text{ 0}\) No distant metastasis
M1 Distant metastasis
M1a Hepatic metastasis(is) only
M1b Extrahepatic metastasis(is) only
M1c Hepatic and extrahepatic metastases

Stage

<table>
<thead>
<tr>
<th>Stage</th>
<th>T</th>
<th>N</th>
<th>M</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>T1</td>
<td>No</td>
<td>Mo</td>
</tr>
<tr>
<td>II</td>
<td>T2, T3</td>
<td>No</td>
<td>Mo</td>
</tr>
<tr>
<td>III</td>
<td>T4</td>
<td>No</td>
<td>Mo</td>
</tr>
<tr>
<td>Any T</td>
<td>N1</td>
<td>Mo</td>
<td></td>
</tr>
<tr>
<td>IV</td>
<td>Any T</td>
<td>Any N</td>
<td>M1</td>
</tr>
</tbody>
</table>

TNM Clinical Classification

Duodenal/Ampullary Tumours

T – Primary Tumour

TX Primary tumour cannot be assessed
To No evidence of primary tumour

T1 Duodenal: Tumour invades mucosa or submucosa and 1 cm or less in greatest dimension

Ampullary: Tumour 1 cm or less in greatest dimension and confined within the sphincter of Oddi

T2 Duodenal: Tumour invades muscularis propria or is more than 1 cm in greatest dimension

Ampullary: Tumour invades through sphincter into duodenal submucosa or muscularis propria, or more than 1 cm in greatest dimension

T3 Tumour invades the pancreas or peripancreatic adipose tissue

T4 Tumour perforates visceral peritoneum (serosa) or invades other organs

Note

For any T, add (m) for multiple tumours.

N – Regional Lymph Nodes

NX Regional lymph nodes cannot be assessed
No No regional lymph node metastasis
N1 Regional lymph node metastasis

M – Distant Metastasis
M0 No distant metastasis  
M1 Distant metastasis  
   M1a Hepatic metastasis(is) only  
   M1b Extrahepatic metastasis(is) only  
   M1c Hepatic and extrahepatic metastases

**Stage**

<table>
<thead>
<tr>
<th>Stage</th>
<th>T</th>
<th>N</th>
<th>M</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>T1</td>
<td>No</td>
<td>M0</td>
</tr>
<tr>
<td>II</td>
<td>T2, T3</td>
<td>No</td>
<td>M0</td>
</tr>
<tr>
<td>III</td>
<td>T4</td>
<td>No</td>
<td>M0</td>
</tr>
<tr>
<td></td>
<td>Any T</td>
<td>N1</td>
<td>M0</td>
</tr>
<tr>
<td>IV</td>
<td>Any T</td>
<td>Any N</td>
<td>M1</td>
</tr>
</tbody>
</table>

**TNM Clinical Classification**

**Jejunum/Ileum**

**T – Primary Tumour**

- TX Primary tumour cannot be assessed
- To No evidence of primary tumour

- T1 Tumour invades lamina propria or submucosa and 1 cm or less in greatest dimension
- T2 Tumour invades muscularis propria or is greater than 1 cm in greatest dimension
- T3 Tumour invades through the muscularis propria into subserosal tissue without penetration of overlying serosa (jejunal or ileal)
- T4 Tumour perforates visceral peritoneum (serosa) or invades other organs or adjacent structures

**Note**

For any T, add (m) for multiple tumours.

**N – Regional Lymph Nodes**

- NX Regional lymph nodes cannot be assessed
- No No regional lymph node metastasis
- N1 Less than 12 regional lymph node metastasis without mesenteric mass(es) greater than 2 cm in sizes
- N2 12 or more regional nodes and/or mesenteric mass(es) greater than 2 cm in sizes
M – Distant Metastasis

M0 No distant metastasis  
M1 Distant metastasis  
  M1a Hepatic metastasis(is) only  
  M1b Extrahepatic metastasis(is) only  
  M1c Hepatic and extrahepatic metastases

Stage

Stage I  T1  No  M0
Stage II  T2, T3  No  M0
Stage III  T4  Any N  M0  
  Any T  N1, N2  M0
Stage IV  Any T  Any N  M1

TNM Clinical Classification

Appendix

T – Primary Tumour\(^a\)

TX Primary tumour cannot be assessed  
To No evidence of primary tumour

T1 Tumour 2 cm or less in greatest dimension  
T2 Tumour more than 2 cm but not more than 4 cm in greatest dimension  
T3 Tumour more than 4 cm or with subserosal invasion or involvement of the mesoappendix  
T4 Tumour perforates peritoneum or invades other adjacent organs or structures, other than direct mural extension to adjacent subserosa, e.g., abdominal wall and skeletal muscle\(^b\)

Notes

\(^a\) High-grade neuroendocrine carcinomas, mixed adenoneuroendocrine carcinomas and goblet cell carcinoid, are excluded and should be classified according to criteria for classifying carcinomas.

\(^b\) Tumour that is adherent to other organs or structures, macroscopically, is classified T4.
However, if no tumour is present in the adhesion, microscopically, the classification should be classified pT1–3.

**N – Regional Lymph Nodes**

- NX Regional lymph nodes cannot be assessed
- No No regional lymph node metastasis
- N1 Regional lymph node metastasis

**M – Distant Metastasis**

- Mo No distant metastasis
- M1 Distant metastasis
  - M1a Hepatic metastasis(is) only
  - M1b Extrahepatic metastasis(is) only
  - M1c Hepatic and extrahepatic metastases

**pTNM Pathological Classification**

The pT and pN categories correspond to the T and N categories. For pM see page 8.

pNo Histological examination of a regional lymphadenectomy specimen will ordinarily include 12 or more lymph nodes. If the lymph nodes are negative, but the number ordinarily examined is not met, classify as pN0.

**Stage**

- Stage I T1 No Mo
- Stage II T2, T3 No Mo
- Stage III T4 No Mo
  - Any T N1 Mo
- Stage IV Any T Any N M1

**TNM Clinical Classification**

*Colon and Rectum*

**T – Primary Tumour**

- TX Primary tumour cannot be assessed
- To No evidence of primary tumour
- T1 Tumour invades lamina propria or submucosa or is no greater than 2 cm in size
T1a   Tumour less than 1 cm in size
T1b   Tumour 1 or 2 cm in size
T2   Tumour invades muscularis propria or is greater than 2 cm in size
T3   Tumour invades subserosa, or non peritonealized pericolic or perirectal tissues
T4   Tumour perforates the visceral peritoneum or invades other organs

Note
For any T, add (m) for multiple tumours.

N – Regional Lymph Nodes

NX  Regional lymph nodes cannot be assessed
No  No regional lymph node metastasis
N1  Regional lymph node metastasis

M – Distant Metastasis

M0  No distant metastasis
M1  Distant metastasis
   M1a  Hepatic metastasis(is) only
   M1b  Extrahepatic metastasis(is) only
   M1c  Hepatic and extrahepatic metastases

pTNM Pathological Classification

The pT and pN categories correspond to the T and N categories. For pM see page 8.

Stage

<table>
<thead>
<tr>
<th>Stage</th>
<th>T</th>
<th>N</th>
<th>M</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage I</td>
<td>T1</td>
<td>N0</td>
<td>M0</td>
</tr>
<tr>
<td>Stage IIA</td>
<td>T2</td>
<td>N0</td>
<td>M0</td>
</tr>
<tr>
<td>Stage IIB</td>
<td>T3</td>
<td>N0</td>
<td>M0</td>
</tr>
<tr>
<td>Stage IIIA</td>
<td>T4</td>
<td>N0</td>
<td>M0</td>
</tr>
<tr>
<td>Stage IIIB</td>
<td>Any T</td>
<td>N1</td>
<td>M0</td>
</tr>
<tr>
<td>Stage IV</td>
<td>Any T</td>
<td>Any N</td>
<td>M1</td>
</tr>
</tbody>
</table>

Well-Differentiated Neuroendocrine Tumours – Pancreas (G1 and G2)

Rules for Classification

This classification system applies to well differentiated neuroendocrine tumours
(carcinoid tumours and atypical carcinoid tumours) of the pancreas.
High-grade neuroendocrine carcinomas are excluded and should be classified according to
criteria for classifying carcinomas of the pancreas.

**Regional lymph nodes**
The regional lymph nodes correspond to those listed under the appropriate sites for
carcinoma.

**TNM Clinical Classification**

**Pancreas**

**T – Primary Tumour**

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>TX</td>
<td>Primary tumour cannot be assessed</td>
</tr>
<tr>
<td>T0</td>
<td>No evidence of primary tumour</td>
</tr>
<tr>
<td>T1</td>
<td>Tumour limited to pancreas, ( b ) 2 cm or less in greatest dimension</td>
</tr>
<tr>
<td>T2</td>
<td>Tumour limited to pancreas, ( b ) more than 2 cm but less than 4 cm in greatest dimension</td>
</tr>
<tr>
<td>T3</td>
<td>Tumour limited to pancreas, ( b ) more than 4 cm in greatest dimension or tumour invading duodenum or bile duct.</td>
</tr>
<tr>
<td>T4</td>
<td>Tumour perforates visceral peritoneum (serosa) or invades other organs or adjacent structures</td>
</tr>
</tbody>
</table>

**Notes**

\( a \) For any T, add (m) for multiple tumours.

\( b \) Invasion of adjacent peripancreatic adipose tissue is accepted but invasion of adjacent organs is excluded.

**N – Regional Lymph Nodes**

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>NX</td>
<td>Regional lymph nodes cannot be assessed</td>
</tr>
<tr>
<td>N0</td>
<td>No regional lymph node metastasis</td>
</tr>
<tr>
<td>N1</td>
<td>Regional lymph node metastasis</td>
</tr>
</tbody>
</table>

**M – Distant Metastasis**

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>M0</td>
<td>No distant metastasis</td>
</tr>
<tr>
<td>M1</td>
<td>Distant metastasis</td>
</tr>
</tbody>
</table>
M1a Hepatic metastasis(is) only
M1b Extrahepatic metastasis(is) only
M1c Hepatic and extrahepatic metastases

<table>
<thead>
<tr>
<th>Stage</th>
<th>T</th>
<th>N</th>
<th>M</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage I</td>
<td>T1</td>
<td>No</td>
<td>Mo</td>
</tr>
<tr>
<td>Stage II</td>
<td>T2, T3</td>
<td>No</td>
<td>Mo</td>
</tr>
<tr>
<td>Stage III</td>
<td>T4</td>
<td>No</td>
<td>Mo</td>
</tr>
<tr>
<td></td>
<td>Any T</td>
<td>N1</td>
<td>Mo</td>
</tr>
<tr>
<td>Stage IV</td>
<td>Any T</td>
<td>Any N</td>
<td>M1</td>
</tr>
</tbody>
</table>
Lung, Pleural, and Thymic Tumours

Introductory Notes

The classifications apply to carcinomas of the lung including non-small cell and small cell carcinomas, bronchopulmonary carcinoid tumours, malignant mesothelioma of pleura, and thymic tumours.

Each site is described under the following headings:
- Rules for classification with the procedures for assessing T, N, and M categories; additional methods may be used when they enhance the accuracy of appraisal before treatment
- Anatomical subsites where appropriate
- Definition of the regional lymph nodes
- TNM clinical classification
- pTNM pathological classification
- Stage
- Prognostic factors grid

Regional Lymph Nodes

The regional lymph nodes extend from the supraclavicular region to the diaphragm. Direct extension of the primary tumour into lymph nodes is classified as lymph node metastasis.

Lung

(ICD-O-3 C34)

Rules for Classification

The classification applies to carcinomas of the lung including non small cell carcinomas, small cell carcinomas, and bronchopulmonary carcinoid tumours. It does not apply to sarcomas and other rare tumours.

Changes in this edition from the seventh edition are based upon recommendations from the International Association for the Study of Lung Cancer (IASLC) Staging Project (see references).

There should be histological confirmation of the disease and division of cases by histological type.
The following are the procedures for assessing T, N, and M categories:

**T categories**  
Physical examination, imaging, endoscopy, and/or surgical exploration

**N categories**  
Physical examination, imaging, endoscopy, and/or surgical exploration

**M categories**  
Physical examination, imaging, and/or surgical exploration

### Anatomical Subsites
1. Main bronchus (C34.0)
2. Upper lobe (C34.1)
3. Middle lobe (C34.2)
4. Lower lobe (C34.3)

### Regional Lymph Nodes
The regional lymph nodes are the intrathoracic nodes (mediastinal, hilar, lobar, interlobar, segmental, and subsegmental), scalene, and supraclavicular lymph nodes.

### TNM Clinical Classification

**T – Primary Tumour**

TX  
Primary tumour cannot be assessed, or tumour proven by the presence of malignant cells in sputum or bronchial washings but not visualized by imaging or bronchoscopy

To  
No evidence of primary tumour

Tis  
Carcinoma in situ

T1  
Tumour 3.0 cm or less in greatest dimension, surrounded by lung or visceral pleura, without bronchoscopic evidence of invasion more proximal than the lobar bronchus (i.e., not in the main bronchus)

T1mi  
Minimally invasive adenocarcinoma

T1a  
Tumour 1.0 cm or less in greatest dimension

T1b  
Tumour more than 1.0 cm but not more than 2.0 cm in greatest dimension

T1c  
Tumour more than 2.0 cm but not more than 3.0 cm in greatest dimension

T2  
Tumour more than 3.0 cm but not more than 5.0 cm; or tumour with any of the following features

- Involves main bronchus regardless of distance to the carina, but without involvement of the carina
- Invades visceral pleura
- Associated with atelectasis or obstructive pneumonitis that extends to the hilar
region either involving part of or the entire lung

T2a  Tumour more than 3.0 cm but not more than 4.0 cm in greatest dimension
T2b  Tumour more than 4.0 cm but not more than 5.0 cm in greatest dimension

T3  Tumour more than 5.0 cm but not more than 7.0 cm in greatest dimension or one that directly invades any of the following: parietal pleura, chest wall (including superior sulcus tumours) phrenic nerve, parietal pericardium; or separate tumour nodule(s) in the same lobe as the primary

T4  Tumour more than 7.0 cm or of any size that invades any of the following: diaphragm, mediastinum, heart, great vessels, trachea, recurrent laryngeal nerve, oesophagus, vertebral body, carina; separate tumour nodule(s) in a different ipsilateral lobe to that of the primary

N – Regional Lymph Nodes

NX Regional lymph nodes cannot be assessed
N0 No regional lymph node metastasis
N1 Metastasis in ipsilateral peribronchial and/or ipsilateral hilar lymph nodes and intrapulmonary nodes, including involvement by direct extension
N2 Metastasis in ipsilateral mediastinal and/or subcarinal lymph node(s)
N3 Metastasis in contralateral mediastinal, contralateral hilar, ipsilateral or contralateral scalene, or supraclavicular lymph node(s)

M – Distant Metastasis

M0 No distant metastasis
M1 Distant metastasis
  M1a Separate tumour nodule(s) in a contralateral lobe; tumour with pleural or pericardial nodules or malignant pleural or pericardial effusion
  M1b Single extrathoracic metastasis in a single organ
  M1c Multiple extrathoracic metastasis in a single or multiple organs

Notes

a Tis includes adenocarcinoma in situ and squamous carcinoma in situ.
b The uncommon superficial spreading tumour of any size with its invasive component limited to the bronchial wall, which may extend proximal to the main bronchus, is also classified as T1a.
c Solitary adenocarcinoma (not more than 3 cm in greatest dimension), with a predominantly lepidic pattern and not more than 5 mm invasion in greatest dimension
T2 tumours with these features are classified T2a if 4 cm or less, or if size cannot be determined and T2b if greater than 4 cm but not larger than 5 cm.

Most pleural (pericardial) effusions with lung cancer are due to tumour. In a few patients, however, multiple microscopic examinations of pleural (pericardial) fluid are negative for tumour, and the fluid is non-bloody and is not an exudate. Where these elements and clinical judgment dictate that the effusion is not related to the tumour, the effusion should be excluded as a staging descriptor.

This includes involvement of a single non-regional node.

**pTNM Pathological Classification**

The pT and pN categories correspond to the T and N categories. For pM see page 8.

pN0 Histological examination of hilar and mediastinal lymphadenectomy specimen(s) will ordinarily include 6 or more lymph nodes/stations. Three of these nodes/stations should be mediastinal, including the subcarinal nodes and three from N1 nodes/stations. Labelling according to the IASLC chart and table of definitions given in the TNM Supplement is desirable. If all the lymph nodes examined are negative, but the number ordinarily examined is not met, classify as pN0.

### Stage

<table>
<thead>
<tr>
<th>Occult carcinoma</th>
<th>TX</th>
<th>No</th>
<th>Mo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage 0</td>
<td>Tis</td>
<td>No</td>
<td>Mo</td>
</tr>
<tr>
<td>Stage IA</td>
<td>T1</td>
<td>No</td>
<td>Mo</td>
</tr>
<tr>
<td>Stage IA1</td>
<td>T1mi</td>
<td>No</td>
<td>Mo</td>
</tr>
<tr>
<td></td>
<td>T1a</td>
<td>No</td>
<td>Mo</td>
</tr>
<tr>
<td>Stage IA2</td>
<td>T1b</td>
<td>No</td>
<td>Mo</td>
</tr>
<tr>
<td>Stage IA3</td>
<td>T1c</td>
<td>No</td>
<td>Mo</td>
</tr>
<tr>
<td>Stage IB</td>
<td>T2a</td>
<td>No</td>
<td>Mo</td>
</tr>
<tr>
<td>Stage IIA</td>
<td>T2b</td>
<td>No</td>
<td>Mo</td>
</tr>
<tr>
<td>Stage IIB</td>
<td>T1a,c,T2a,b</td>
<td>N1</td>
<td>Mo</td>
</tr>
<tr>
<td></td>
<td>T3</td>
<td>No</td>
<td>Mo</td>
</tr>
<tr>
<td>Stage IIIA</td>
<td>T1a.c, T2a,b</td>
<td>N2</td>
<td>Mo</td>
</tr>
<tr>
<td></td>
<td>T3</td>
<td>N1</td>
<td>Mo</td>
</tr>
<tr>
<td></td>
<td>T4</td>
<td>No, N1</td>
<td>Mo</td>
</tr>
<tr>
<td>Stage IIIB</td>
<td>T1a.c, T2a,b</td>
<td>N3</td>
<td>Mo</td>
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Prognostic Factors Grid – Non-Small Cell Lung Carcinoma

Prognostic factors in surgically resected NSCLC

<table>
<thead>
<tr>
<th>Prognostic factors</th>
<th>Tumour related</th>
<th>Host related</th>
<th>Environment related</th>
</tr>
</thead>
<tbody>
<tr>
<td>Essential</td>
<td>T category N category Extracapsular nodal extension</td>
<td>Weight loss Performance status</td>
<td>Resection margins Adequacy of mediastinal dissection</td>
</tr>
<tr>
<td>Additional</td>
<td>Histological type Grade Vessel invasion Tumour size</td>
<td>Gender</td>
<td></td>
</tr>
<tr>
<td>New and promising</td>
<td>Molecular/biological markers</td>
<td>Quality of life Marital status</td>
<td></td>
</tr>
</tbody>
</table>

Prognostic risk factors in advanced (locally advanced or metastatic) NSCLC

<table>
<thead>
<tr>
<th>Prognostic factors</th>
<th>Tumour related</th>
<th>Host related</th>
<th>Environment related</th>
</tr>
</thead>
<tbody>
<tr>
<td>Essential</td>
<td>Stage Superior vena cava obstruction (SVCO) Oligometastatic disease Number of sites</td>
<td>Weight loss Performance status</td>
<td>Chemotherapy Targeted therapy</td>
</tr>
<tr>
<td>Additional</td>
<td>Number of metastatic sites Pleural effusion Liver metastasis Haemoglobin Lactate dehydrogenase (LDH) Albumin</td>
<td>Gender Symptom burden</td>
<td></td>
</tr>
<tr>
<td>New and promising</td>
<td>Molecular/biological markers</td>
<td>Quality of life Marital status Anxiety/depression</td>
<td></td>
</tr>
</tbody>
</table>


Prognostic Factors Grid – Small Cell Lung Carcinoma
Prognostic risk factors in SCLC

<table>
<thead>
<tr>
<th>Prognostic factors</th>
<th>Tumour related</th>
<th>Host related</th>
<th>Environment related</th>
</tr>
</thead>
<tbody>
<tr>
<td>Essential</td>
<td>Stage</td>
<td>Performance status</td>
<td>Thoracic radiotherapy</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Age</td>
<td>Chemotherapy</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Comorbidity</td>
<td></td>
</tr>
<tr>
<td>Additional</td>
<td>LDH</td>
<td>Chemotherapy</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Thoracic</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>radiotherapy</td>
<td></td>
</tr>
<tr>
<td>New and promising</td>
<td>Molecular/biological markers</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Alkaline phosphatase Cushing syndrome M0 – mediastinal involvement M1 – number of sites Brain or bone involvement White blood cell count (WBC)/platelet count


References


**Pleural Mesothelioma**

(ICD-O C38.4)

**Rules for Classification**

The classification applies only to malignant mesothelioma of the pleura. There should be histological confirmation of the disease.

*Changes in this edition from the seventh edition are based upon recommendations from the International Association for the Study of Lung Cancer (IASLC) Staging Project.*

The following are the procedures for assessing T, N, and M categories:

- **T categories**  
  Physical examination, imaging, endoscopy, and/or surgical exploration
- **N categories**  
  Physical examination, imaging, endoscopy, and/or surgical exploration
- **M categories**  
  Physical examination, imaging, and/or surgical exploration

**Regional Lymph Nodes**

The regional lymph nodes are the intrathoracic, internal mammary, scalene, and supraclavicular nodes.

**TNM Clinical Classification**

**T – Primary Tumour**

- **TX** Primary tumour cannot be assessed
- **T0** No evidence of primary tumour
- **T1** Tumour involves ipsilateral parietal or visceral pleura only, with or without involvement of visceral, mediastinal or diaphragmatic pleura.
- **T2** Tumour involves the ipsilateral pleura (parietal or visceral pleura), with at least one of the following:
  - invasion of diaphragmatic muscle
  - invasion of lung parenchyma
- **T3** Tumour involves ipsilateral pleura (parietal or visceral pleura), with at least one of the following:
  - invasion of endo thoracic fascia
  - invasion into mediastinal fat
solitary focus of tumour invading soft tissues of the chest wall
- non-transmural involvement of the pericardium

T4. Tumour involves ipsilateral pleura (parietal or visceral pleura), with at least one of the following:
- chest wall, with or without associated rib destruction (diffuse or multifocal)
- peritoneum (via direct transdiaphragmatic extension)
- contralateral pleura
- mediastinal organs (oesophagus, trachea, heart, great vessels)
- vertebra, neuroforamen, spinal cord
- internal surface of the pericardium (transmural invasion with or without a pericardial effusion)

N – Regional Lymph Nodes

NX Regional lymph nodes cannot be assessed
N0 No regional lymph node metastasis
N1 Metastases to ipsilateral intrathoracic lymph nodes (includes ipsilateral bronchopulmonary, hilar, subcarinal, paratracheal, aortopulmonary, paraesophageal, peridiaphragmatic, pericardial fat pad, intercostal and internal mammary nodes)
N2 Metastases to contralateral intrathoracic lymph nodes. Metastases to ipsilateral or contralateral supraclavicular lymph nodes

M – Distant Metastasis

M0 No distant metastasis
M1 Distant metastasis

pTNM Pathological Classification

The pT and pN categories correspond to the T and N categories. For pM see page 8.

Stage – Pleural Mesothelioma

<table>
<thead>
<tr>
<th>Stage</th>
<th>pT</th>
<th>pN</th>
<th>pM</th>
</tr>
</thead>
<tbody>
<tr>
<td>IA</td>
<td>T1</td>
<td>No</td>
<td>Mo</td>
</tr>
<tr>
<td>IB</td>
<td>T2,T3</td>
<td>No</td>
<td>Mo</td>
</tr>
<tr>
<td>II</td>
<td>T1,T2</td>
<td>N1</td>
<td>Mo</td>
</tr>
<tr>
<td>IIIA</td>
<td>T3</td>
<td>N1</td>
<td>Mo</td>
</tr>
<tr>
<td>IIIB</td>
<td>T1,T2,T3</td>
<td>N2</td>
<td>Mo</td>
</tr>
<tr>
<td></td>
<td>T4</td>
<td>Any N</td>
<td>Mo</td>
</tr>
</tbody>
</table>
Thymic Tumours

ICD-O-3 C37.9

Rules for Classification

The classification applies to epithelial tumours of the thymus, including thymomas, thymic carcinomas and neuroendocrine tumours of the thymus. It does not apply to sarcomas, lymphomas and other rare tumours.

This classification is new to the 8th edition and is based upon recommendations from the International Association for the Study of Lung Cancer (IASLC) Staging Project and the International Thymic Malignancies Interest Group (ITMIG) (see references).1–3

There should be histological confirmation of the disease and division of cases by histological type.

The following are the procedures for assessing T, N, and M categories:

T categories  Physical examination, imaging, endoscopy, and/or surgical exploration

N categories  Physical examination, imaging, endoscopy, and/or surgical exploration

M categories  Physical examination, imaging, and/or surgical exploration

Regional Lymph Nodes

The regional lymph nodes are the anterior (perithymic) lymph nodes, the deep intrathoracic lymph nodes and the cervical lymph nodes.

TNM Clinical Classification

T – Primary Tumour

TX Primary tumour cannot be assessed

To No evidence of primary tumour

T1 Tumour encapsulated or extending into the mediastinal fat, may involve the mediastinal pleura.

T1a No mediastinal pleural involvement

T1b Direct invasion of the mediastinal pleura

T2 Tumour with direct involvement of the pericardium (partial or full thickness).

T3 Tumour with direct invasion into any of the following; lung, brachiocephalic vein, superior vena cava, phrenic nerve, chest wall, or extrapericardial pulmonary artery or
T4 Tumour with direct invasion into any of the following; aorta (ascending, arch or descending), arch vessels, intrapericardial pulmonary artery, myocardium, trachea, or oesophagus

N – Regional Lymph Nodes

NX Regional lymph nodes cannot be assessed
No No regional lymph node metastasis
N1 Metastasis in anterior (perithymic) lymph nodes
N2 Metastasis in deep intrathoracic or cervical lymph nodes

M – Distant Metastasis

Mo No pleural, pericardial or distant metastasis
M1 Distant metastasis
M1a Separate pleural or pericardial nodule(s)
M1b Distant metastasis beyond the pleura or pericardium

TNM Pathological Classification

The pT and pN categories correspond to the T and N categories. For pM see page 8.

Stage – THYMUS TUMOURS

Stage I   T1   No   Mo
Stage II  T2   No   Mo
Stage IIIA T3  No   Mo
Stage IIIB T4  No   Mo
Stage IVA Any T N1   Mo
Any T No, N1 M1a
Stage IVB Any T N2   Mo, M1a
Any T Any N  M1b

References


Tumours of Bone and Soft Tissues

Introductory Notes

The following sites are included:

- Bone
- Soft tissues
- Gastrointestinal stromal tumours

Each site is described under the following headings:

- Rules for classification with the procedures for assessing T, N, and M categories; additional methods may be used when they enhance the accuracy of appraisal before treatment
- Anatomical sites where appropriate
- Definition of the regional lymph nodes
- TNM clinical classification
- pTNM pathological classification
- G histopathological grading
- Stage
- Prognostic factors grid

G Histopathological Grading

The staging of bone and soft tissue sarcomas is based on a three-tiered grade classification. In this classification, Grade 1 is considered ‘low grade’ and Grades 2 and 3 ‘high grade’.

Bone

(ICD-O-3 C40, 41)

Rules for Classification

The classification applies to all primary malignant bone tumours except malignant lymphoma, multiple myeloma, surface/juxtacortical osteosarcoma, and juxtacortical chondrosarcoma. There should be histological confirmation of the disease and division of cases by histological type and grade.

The following are the procedures for assessing T, N, and M categories:
Regional Lymph Nodes

The regional lymph nodes are those appropriate to the site of the primary tumour. Regional node involvement is rare and cases in which nodal status is not assessed either clinically or pathologically could be considered No instead of NX or pNX.

TNM Clinical Classification

T – Primary Tumour

- TX Primary tumour cannot be assessed
- T0 No evidence of primary tumour

Appendicular Skeleton, Trunk, Skull and Facial Bones

- T1 Tumour 8 cm or less in greatest dimension
- T2 Tumour more than 8 cm in greatest dimension
- T3 Discontinuous tumours in the primary bone site

Spine

- T1 Tumour confined to a single vertebral segment or two adjacent vertebral segments
- T2 Tumour confined to three adjacent vertebral segments
- T3 Tumour confined to four adjacent vertebral segments
- T4a Tumour invades into the spinal canal
- T4b Tumour invades the adjacent vessels or tumour thrombosis within the adjacent vessels

Notes

The five vertebral segments are the:

- Right pedicle
- Right body
- Left body
- Left pedicle
- Posterior element

Pelvis
T1a A tumour 8 cm or less in size and confined to a single pelvic segment with no extraosseous extension

T1b A tumour greater than 8 cm in size and confined to a single pelvic segment with no extraosseous extension

T2a A tumour 8 cm or less in size and confined to a single pelvic segment with extraosseous extension or confined to two adjacent pelvic segments without extraosseous extension

T2b A tumour greater than 8 cm in size and confined to a single pelvic segment with extraosseous extension or confined to two adjacent pelvic segments without extraosseous extension

T3a A tumour 8 cm or less in size and confined to two pelvic segments with extraosseous extension

T3b A tumour greater than 8 cm in size and confined to two pelvic segments with extraosseous extension

T4a Tumour involving three adjacent pelvic segments or crossing the sacroiliac joint to the sacral neuroforamen

T4b Tumour encasing the external iliac vessels or gross tumour thrombus in major pelvic vessels

**Note**

The four pelvic segments are the:

- Sacrum lateral to the sacral foramen,
- Iliac wing,
- Acetabulum/periacetabulum and
- Pelvic rami, symphysis and ischium

**N – Regional Lymph Nodes**

- NX Regional lymph nodes cannot be assessed
- No No regional lymph node metastasis
- N1 Regional lymph node metastasis

**M – Distant Metastasis**

- Mo No distant metastasis
- M1 Distant metastasis
  - M1a Lung
  - M1b Other distant sites
PTNM Pathological Classification

The pT and pN categories correspond to the T and N categories. For pM see page 8.

Stage – Appendicular Skeleton, Trunk, Skull and Facial Bones

<table>
<thead>
<tr>
<th>Stage</th>
<th>T</th>
<th>N</th>
<th>M</th>
<th>Grade</th>
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</thead>
<tbody>
<tr>
<td>Stage IA</td>
<td>T1</td>
<td>N0</td>
<td>M0</td>
<td>G1, GX Low Grade</td>
</tr>
<tr>
<td>Stage IB</td>
<td>T2, T3</td>
<td>N0</td>
<td>M0</td>
<td>G1, GX Low Grade</td>
</tr>
<tr>
<td>Stage IIA</td>
<td>T1</td>
<td>N0</td>
<td>M0</td>
<td>G2, G3 High Grade</td>
</tr>
<tr>
<td>Stage IIB</td>
<td>T2</td>
<td>N0</td>
<td>M0</td>
<td>G2, G3 High Grade</td>
</tr>
<tr>
<td>Stage III</td>
<td>T3</td>
<td>N0</td>
<td>M0</td>
<td>G2, G3 High Grade</td>
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<td>Stage IVA</td>
<td>Any T</td>
<td>N0</td>
<td>M1a</td>
<td>Any G</td>
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<td>N0</td>
<td>M1b</td>
<td>Any G</td>
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</table>

Stage – Spine and Pelvis

There is no stage for bone sarcomas of the spine or pelvis.

Prognostic Factors Grid – Bone

Prognostic factors for osteosarcoma

<table>
<thead>
<tr>
<th>Prognostic factors</th>
<th>Tumour related</th>
<th>Host related</th>
<th>Environment related</th>
</tr>
</thead>
<tbody>
<tr>
<td>Essential</td>
<td>Location, size, extent of disease</td>
<td>Age</td>
<td>Residual disease after resection</td>
</tr>
<tr>
<td></td>
<td>Tumour response to neoadjuvant chemotherapy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Additional</td>
<td>LDH Alkaline phosphatase</td>
<td>Gender Performance status</td>
<td>Management by a multidisciplinary sarcoma team Local recurrence</td>
</tr>
<tr>
<td>New and promising</td>
<td>Biomarkers</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>


Soft Tissues

(ICD-O-3 C38.1, 2, C47-49)

Rules for Classification
There should be histological confirmation of the disease and division of cases by histological type and grade.

The following are the procedures for assessing T, N, and M categories:

- **T categories** Physical examination and imaging
- **N categories** Physical examination and imaging
- **M categories** Physical examination and imaging

**Anatomical Sites**

1. Connective, subcutaneous, and other soft tissues (C49), peripheral nerves (C47)
2. Retroperitoneum (C48.0)
3. Mediastinum: anterior (C38.1); posterior (C38.2); mediastinum, NOS (C38.3)

**Histological Types of Tumour**

The following histological types are not included:

- Kaposi sarcoma
- Dermatofibrosarcoma (protuberans)
- Fibromatosis (desmoid tumour)
- Sarcoma arising from the dura mater, brain, hollow viscera, or parenchymatous organs (with the exception of breast sarcomas)
- Angiosarcoma, an aggressive sarcoma, is excluded because its natural history is not consistent with the classification.

**Regional Lymph Nodes**

The regional lymph nodes are those appropriate to the site of the primary tumour. Regional node involvement is rare and cases in which nodal status is not assessed either clinically or pathologically could be considered N0 instead of NX or pNX.

**TNM Clinical Classification**

**T – Primary Tumour**

- **TX** Primary tumour cannot be assessed
- **T0** No evidence of primary tumour

**Extremity and Superficial Trunk**

- **T1** Tumour 5 cm or less in greatest dimension
- **T2** Tumour more than 5 cm but no more than 10 cm in greatest dimension
T3 Tumour more than 10.0cm but no more than 15.0cm in greatest dimension
T4 Tumour more than 15.0cm in greatest dimension

**Retroperitoneum**

T1 Tumour 5.0cm or less in greatest dimension
T2 Tumour more than 5.0cm but no more than 10.0cm in greatest dimension
T3 Tumour more than 10.0cm but no more than 15.0cm in greatest dimension
T4 Tumour more than 15.0cm in greatest dimension

**Head and Neck**

T1 Tumour 2.0cm or less in greatest dimension
T2 Tumour more than 2.0cm but no more than 4.0cm in greatest dimension
T3 Tumour more than 4.0cm in greatest dimension
T4a Tumour invades the orbit, skull base or dura, central compartment viscera, facial skeleton, and or pterygoid muscles
T4b Tumour invades the brain parenchyma, encases the carotid artery, invades prevertebral muscle or involves the central nervous system by perineural spread

**Thoracic and Abdominal Viscera**

T1 Tumour confined to a single organ
T2a Tumour invades serosa or visceral peritoneum
T2b Tumour with microscopic extension beyond the serosa
T3 Tumour invades another organ or macroscopic extension beyond the serosa
T4a Multifocal tumour involving no more than two sites in one organ
T4b Multifocal tumour involving more than two sites but not more then 5 sites
T4c Multifocal tumour involving more than five sites

**N – Regional Lymph Nodes**

NX Regional lymph nodes cannot be assessed
N0 No regional lymph node metastasis
N1 Regional lymph node metastasis

**M – Distant Metastasis**

MO No distant metastasis
M1 Distant metastasis

**pTNM Pathological Classification**
Stage – Extremity and Superficial Trunk and Retroperitoneum

<table>
<thead>
<tr>
<th>Stage</th>
<th>T</th>
<th>N</th>
<th>M</th>
<th>Grade</th>
</tr>
</thead>
<tbody>
<tr>
<td>IA</td>
<td>T1</td>
<td>No</td>
<td>M0</td>
<td>G1, GX Low Grade</td>
</tr>
<tr>
<td>IB</td>
<td>T2, T3, T4</td>
<td>No</td>
<td>M0</td>
<td>G1, GX Low Grade</td>
</tr>
<tr>
<td>II</td>
<td>T1</td>
<td>No</td>
<td>M0</td>
<td>G2, G3 High Grade</td>
</tr>
<tr>
<td>IIIA</td>
<td>T2</td>
<td>No</td>
<td>M0</td>
<td>G2, G3 High Grade</td>
</tr>
<tr>
<td>IIIB</td>
<td>T3, T4</td>
<td>No</td>
<td>M0</td>
<td>G2, G3 High Grade</td>
</tr>
<tr>
<td>IIIB</td>
<td>Any T</td>
<td>N1*</td>
<td>M0</td>
<td>Any G</td>
</tr>
<tr>
<td>IV</td>
<td>Any T</td>
<td>Any N</td>
<td>M1</td>
<td>Any G</td>
</tr>
</tbody>
</table>

Note
* AJCC classifies N1 as stage IV for extremity and superficial trunk.

Stage – Head and Neck and Thoracic and Abdominal Viscera

There is no stage for soft tissue sarcoma of the head and neck and thoracic and abdominal viscera.

Gastrointestinal Stromal Tumour (GIST)

Rules for Classification

The classification applies only to gastrointestinal stromal tumours. There should be histological confirmation of the disease.

The following are the procedures for assessing the T, N, and M categories.

\[ T \text{ categories} \quad \text{Physical examination, imaging, endoscopy, and/or surgical exploration} \]
\[ N \text{ categories} \quad \text{Physical examination, imaging, and/or surgical exploration} \]
\[ M \text{ categories} \quad \text{Physical examination, imaging, and/or surgical exploration} \]

Anatomical Sites and Subsites

- Oesophagus (C15)
- Stomach (C16)
- Small intestine (C17)
  1. Duodenum (C17.0)
Regional Lymph Nodes
The regional lymph nodes are those appropriate to the site of the primary tumour; see gastrointestinal sites for details.

TNM Clinical Classification

T – Primary Tumour

TX Primary tumour cannot be assessed
To No evidence for primary tumour
T1 Tumour 2.0 cm or less
T2 Tumour more than 2.0 cm but not more than 5.0 cm
T3 Tumour more than 5.0 cm but not more than 10.0 cm
T4 Tumour more than 10.0 cm in greatest dimension

N – Regional Lymph Nodes

NX Regional lymph nodes cannot be assessed*
No No regional lymph node metastasis
N1 Regional lymph node metastasis

Note
* NX: Regional lymph node involvement is rare for GISTs, so that cases in which the nodal status is not assessed clinically or pathologically could be considered No instead of NX or pNX.

M – Distant Metastasis

Mo No distant metastasis
M1 Distant metastasis

pTNM Pathological Classification
G Histopathological Grading

Grading for GIST is dependent on mitotic rate. *

Low mitotic rate: 5 or fewer per 50 hpf
High mitotic rate: over 5 per 50 hpf

Note

* The mitotic rate of GIST is best expressed as the number of mitoses per 50 high power fields (hpf) using the 40× objective (total area 5 mm² in 50 fields).

Stage

Staging criteria for gastric tumours can be applied in primary, solitary omental GISTs. Staging criteria for intestinal tumours can be applied to GISTs in less common sites such as oesophagus, colon, rectum, and mesentery.

Gastric GIST

<table>
<thead>
<tr>
<th>Stage</th>
<th>Mitotic rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>IA</td>
<td>T1, T2</td>
</tr>
<tr>
<td>IB</td>
<td>T3</td>
</tr>
<tr>
<td>II</td>
<td>T1, T2</td>
</tr>
<tr>
<td></td>
<td>T4</td>
</tr>
<tr>
<td>IIIA</td>
<td>T3</td>
</tr>
<tr>
<td>IIIB</td>
<td>T4</td>
</tr>
<tr>
<td>IV</td>
<td>Any T</td>
</tr>
<tr>
<td></td>
<td>Any T</td>
</tr>
</tbody>
</table>

Small Intestinal GIST

<table>
<thead>
<tr>
<th>Stage</th>
<th>Mitotic rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>T1, T2</td>
</tr>
<tr>
<td>II</td>
<td>T3</td>
</tr>
<tr>
<td>IIIA</td>
<td>T1</td>
</tr>
<tr>
<td></td>
<td>T4</td>
</tr>
<tr>
<td>IIIB</td>
<td>T2, T3, T4</td>
</tr>
<tr>
<td>IV</td>
<td>Any T</td>
</tr>
</tbody>
</table>
## Prognostic Factor Grid – Soft Tissue Sarcoma and GIST

Prognostic factors for soft tissue sarcomas

<table>
<thead>
<tr>
<th>Prognostic factors</th>
<th>Tumour related</th>
<th>Host related</th>
<th>Environment related</th>
</tr>
</thead>
</table>
| Essential          | Anatomical site  
|                    | Histological type  
|                    | Size of tumour:  
|                    | - < or > 5 cm in general  
|                    | - ≤2, 2–≤5, 5–≤10 and >10 cm for GIST  
|                    | Depth of invasion Grade (well to poorly differentiated)  
|                    | M category  
|                    | Mitotic rate for GIST (<5 mitoses and ≥5 mitoses/50 HPF)  |
| Additional         | Presence of *c* *Kit* mutation for GIST  
|                    | Mutational site in *c* *Kit* or *PDGFRA* gene for GIST  
|                    | *EWS–FL11* fusion transcript for Ewing sarcoma  
|                    | *SYT–SSX* fusion transcript for synovial sarcoma  
|                    | *FOXO1* translocation for alveolar rhabdomyosarcoma  
|                    | Surgical resection margins  
|                    | Presentation status (primary vs recurrence)  |
| New and promising  | *TP53* *Ki67*  
|                    | Tumour hypoxia  |

Skin Tumours

Introductory Notes

The classifications apply to: carcinomas of the skin,* [excluding vulva (see page 161), penis (see page 188), and perianal skin (see page 77)], malignant melanomas of the skin including eyelid, and to Merkel cell carcinoma.

Note

* There is a new classification for carcinoma of the skin of the head and neck region.

Anatomical Sites

The following sites are identified by ICD.O.3 topography rubrics:

- Lip (excluding vermilion surface) (C44.0)
- Eyelid (C44.1)
- External ear (C44.2)
- Other and unspecified parts of face (C44.3)
- Scalp and neck (C44.4)
- Trunk excluding anal margin and perianal skin (C44.5)
- Upper limb and shoulder (C44.6)
- Lower limb and hip (C44.7)
- Scrotum (C63.2)

Each tumour type is described under the following headings:

- Rules for classification with the procedures for assessing T, N, and M categories
- Regional lymph nodes
- TNM clinical classification
- pTNM pathological classification
- Stage
- Prognostic factors grid

Regional Lymph Nodes

The regional lymph nodes are those appropriate to the site of the primary tumour.
Unilateral Tumours

- **Head, neck:** Ipsilateral preauricular, submandibular, cervical, and supraclavicular lymph nodes
- **Thorax:** Ipsilateral axillary lymph nodes
- **Upper limb:** Ipsilateral epitrochlear and axillary lymph nodes
- **Abdomen, loins, and buttocks:** Ipsilateral inguinal lymph nodes
- **Lower limb:** Ipsilateral popliteal and inguinal lymph nodes

Tumours in the Boundary Zones Between these sites

The lymph nodes pertaining to the regions on both sides of the boundary zone are considered to be the regional lymph nodes. The following 4 cm wide bands are considered as boundary zones:

<table>
<thead>
<tr>
<th>Between</th>
<th>Along</th>
</tr>
</thead>
<tbody>
<tr>
<td>Right/left</td>
<td>Midline</td>
</tr>
<tr>
<td>Head and neck/thorax</td>
<td>Clavica–acromion–upper shoulder blade edge</td>
</tr>
<tr>
<td>Thorax/upper limb</td>
<td>Shoulder–axilla–shoulder</td>
</tr>
<tr>
<td>Thorax/abdomen, loins, and buttocks</td>
<td><em>Front:</em> middle between navel and costal arch</td>
</tr>
<tr>
<td></td>
<td><em>Back:</em> lower border of thoracic vertebrae (midtransverse axis)</td>
</tr>
<tr>
<td>Abdomen, loins, and buttock/lower limb</td>
<td>Groin–trochanter–gluteal Sulcus</td>
</tr>
</tbody>
</table>

Any metastasis to other than the listed regional lymph nodes is considered as M1.

Carcinoma of Skin (excluding eyelid, head and neck, perianal, vulva, and penis)

(ICD-O-3 C44.5-7, C63.2)*

Rules for Classification*

The classification applies only to carcinomas, excluding Merkel cell carcinoma. There should be histological confirmation of the disease and division of cases by histological type.

The following are the procedures for assessing T, N, and M categories:
**T categories**  Physical examination

**N categories**  Physical examination and imaging

**M categories**  Physical examination and imaging

**Note**

* The AJCC only includes the classification for skin carcinoma of the head and neck.

**Regional Lymph Nodes**

The regional lymph nodes are those appropriate to the site of the primary tumour. See page 132.

**TNM Clinical Classification**

**T – Primary Tumour**

- TX  Primary tumour cannot be identified
- T0  No evidence of primary tumour
- Tis  Carcinoma in situ

T1  Tumour 2 cm or less in greatest dimension
T2  Tumour >2 cm and ≤4 cm in greatest dimension
T3  Tumour >4 cm in greatest dimension or minor bone erosion or perineural invasion or deep invasion*
T4a Tumour with gross cortical bone/marrow invasion
T4b Tumour with axial skeleton invasion including foraminal involvement and/or vertebral foramen involvement to the epidural space

**Note**

* Deep invasion is defined as invasion beyond the subcutaneous fat or >6 mm (as measured from the granular layer of adjacent normal epidermis to the base of the tumour); perineural invasion for T3 classification is defined as clinical or radiographic involvement of named nerves without foramen or skull base invasion or transgression.

In the case of multiple simultaneous tumours, the tumour with the highest T category is classified and the number of separate tumours is indicated in parentheses, e.g., T2(5).

**N – Regional Lymph Nodes**

NX  Regional lymph nodes cannot be assessed
No  No regional lymph node metastasis
N1 Metastasis in a single lymph node 3 cm or less in greatest dimension
N2 Metastasis in a single ipsilateral lymph node, more than 3 cm but not more than 6 cm in greatest dimension or in multiple ipsilateral nodes none more than 6 cm in greatest dimension
N3 Metastasis in a lymph node more than 6 cm in greatest dimension

M – Distant Metastasis

M0 No distant metastasis
M1 Distant metastatic disease*

Note

* Contralateral nodes in non-melanoma non-head and neck cancer are distant metastases.

pTNM Pathological Classification

The pT and pN categories correspond to the T and N categories. For pM see page 8.
pN0 Histological examination of a regional lymphadenectomy specimen will ordinarily include 6 or more lymph nodes. If the lymph nodes are negative, but the number ordinarily examined is not met, classify as pN0.

Stage

<table>
<thead>
<tr>
<th>Stage</th>
<th>T</th>
<th>N</th>
<th>M</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Tis</td>
<td>No</td>
<td>Mo</td>
</tr>
<tr>
<td>I</td>
<td>T1</td>
<td>No</td>
<td>Mo</td>
</tr>
<tr>
<td>II</td>
<td>T2</td>
<td>No</td>
<td>Mo</td>
</tr>
<tr>
<td>III</td>
<td>T3</td>
<td>No</td>
<td>Mo</td>
</tr>
<tr>
<td></td>
<td>T1, T2, T3 N1</td>
<td></td>
<td>Mo</td>
</tr>
<tr>
<td>IVA</td>
<td>T1, T2, T3 N2, N3 Mo</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>T4</td>
<td>Any N</td>
<td>Mo</td>
</tr>
<tr>
<td>IVB</td>
<td>Any T</td>
<td>Any N</td>
<td>M1</td>
</tr>
</tbody>
</table>

Prognostic Factors Grid – Non-Melanoma Skin
Tumour-, host- and environment-related prognostic factors for skin cancer

<table>
<thead>
<tr>
<th>Prognostic factors</th>
<th>Tumour related</th>
<th>Host related</th>
<th>Environment related</th>
</tr>
</thead>
<tbody>
<tr>
<td>Essential</td>
<td>TNM</td>
<td>Immune suppression</td>
<td>Surgical margins Previous RT</td>
</tr>
<tr>
<td></td>
<td>Histopathological type Location Thickness PNI (clinical)</td>
<td>Recurrent disease</td>
<td></td>
</tr>
<tr>
<td>Additional</td>
<td>Tumour borders Differentiation Rate of growth LVSI PNI (incidental)</td>
<td>Genetic factors Gorlin syndrome Age</td>
<td>Smoking (SCC)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Chronic inflammation, scars, burns</td>
<td></td>
</tr>
<tr>
<td>New and promising</td>
<td>SLNB Perturbed cellular pathways</td>
<td></td>
<td>Viral aetiology Highly conformal RT</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Chemoradiotherapy Targeted therapies Intralesional therapy</td>
</tr>
</tbody>
</table>


Skin Carcinoma of the Head and Neck

(ICD-O-3 C44.0 C44.2-4)

Rules for Classification

The classification applies only to cutaneous carcinomas of the head and neck region excluding the eyelid and excluding Merkel cell carcinoma and malignant melanoma. There should be histological confirmation of the disease.

The following are the procedures for assessing T, N, and M categories:

*T categories*  Physical examination and imaging

*N categories*  Physical examination and imaging

*M categories*  Physical examination and imaging

Anatomical Sites

The following sites are identified by ICD.O topography rubrics:

- Lip (excluding vermilion surface) (C44.0)
- External ear (C44.2)
- Other and unspecified parts of face (C44.3)
- Scalp and neck (C44.4)

**TNM Clinical Classification**

**T – Primary Tumour**

- **TX** Primary tumour cannot be identified
- **To** No evidence of primary tumour
- **Tis** Carcinoma in situ

- **T1** Tumour 2 cm or less in greatest dimension
- **T2** Tumour >2 cm and ≤4 cm in greatest dimension
- **T3** Tumour >4 cm in greatest dimension or minor bone erosion or perineural invasion or deep invasion*
- **T4a** Tumour with gross cortical bone/marrow invasion
- **T4b** Tumour with skull base or axial skeleton invasion including foraminal involvement and/or vertebral foramen involvement to the epidural space

**Note**

*Deep invasion is defined as invasion beyond the subcutaneous fat or >6 mm (as measured from the granular layer of adjacent normal epidermis to the base of the tumour), perineural invasion for T3 classification is defined as clinical or radiographic involvement of named nerves without foramen or skull base invasion or transgression.

**N – Regional Lymph Nodes**

- **No** No regional lymph node metastasis
- **N1** Metastasis in a single ipsilateral lymph node, 3 cm or less in greatest dimension without extranodal extension
- **N2** Metastasis described as:
  - **N2a** Metastasis in a single ipsilateral lymph node more than 3 cm but not more than 6 cm in greatest dimension without extranodal extension
  - **N2b** Metastasis in multiple ipsilateral lymph nodes, none more than 6 cm in greatest dimension, without extranodal extension
  - **N2c** Metastasis in bilateral or contralateral lymph nodes, none more than 6 cm in greatest dimension, without extranodal extension
- **N3a** Metastasis in a lymph node more than 6 cm in greatest dimension without extranodal extension
N3b Metastasis in a single or multiple lymph nodes with clinical extranodal extension

**Note**

* The presence of skin involvement or soft tissue invasion with deep fixation/tethering to underlying muscle or adjacent structures or clinical signs of nerve involvement is classified as clinical extranodal extension.

**M – Distant Metastasis**

M0 No distant metastasis  
M1 Distant metastasis

**pTNM Pathological Classification**

The pT categories correspond to the clinical T categories. For pM see page 8.

**pN – Regional Lymph Nodes**

Histological examination of a selective neck dissection specimen will ordinarily include 10 or more lymph nodes. Histological examination of a radical or modified radical neck dissection specimen will ordinarily include 15 or more lymph nodes.

pNX Regional lymph nodes cannot be assessed  
pN0 No regional lymph node metastasis  
pN1 Metastasis in a single ipsilateral lymph node, 3 cm or less in greatest dimension without extranodal extension  
pN2 Metastasis described as:
  
pN2a Metastasis in a single ipsilateral lymph node, less than 3 cm in greatest dimension with extranodal extension or, more than 3 cm but not more than 6 cm in greatest dimension without extranodal extension  
pN2b Metastasis in multiple ipsilateral lymph nodes, none more than 6 cm in greatest dimension, without extranodal extension  
pN2c Metastasis in bilateral or contralateral lymph nodes, none more than 6 cm in greatest dimension, without extranodal extension  
pN3a Metastasis in a lymph node more than 6 cm in greatest dimension without extranodal extension  
pN3b Metastasis in a lymph node more than 3 cm in greatest dimension with extranodal extension or multiple ipsilateral, or any contralateral or bilateral node(s) with extranodal extension

**Stage**
Carcinoma of Skin of the Eyelid

(ICD-O C44.1)

Rules of Classification

There should be histological confirmation of the disease and division of cases by histological type – for example, basal cell, squamous cell, sebaceous carcinoma. Melanoma of the eyelid is classified with skin tumours, see page 142.

The following are procedures for assessing T, N, and M categories:

- **T categories**  Physical examination
- **N categories**  Physical examination
- **M categories**  Physical examination and imaging

Regional Lymph Nodes

The regional lymph nodes are the preauricular, submandibular, and cervical lymph nodes.

TNM Clinical Classification

T – Primary Tumour

- **T0**  No evidence of primary tumour
- **Tis**  Carcinoma in situ

T1  Tumour 10 mm or less in greatest dimension

- **T1a**  Not invading the tarsal plate or eyelid margin
- **T1b**  Invades tarsal plate or eyelid margin
- **T1c**  Involves full thickness of eyelid

T2  Tumour >10 mm, but 20 mm or less in greatest dimension

- **T2a**  Not invading the tarsal plate or eyelid margin
- **T2b**  Invades tarsal plate or eyelid margin
- **T2c**  Involves full thickness of eyelid
T2b Invades the tarsal plate or eyelid margin
T2c Involves full thickness of eyelid
T3 Tumour > 20 mm, but more than 30 mm in greatest dimension
  T3a Not invading the tarsal plate or eyelid margin
  T3b Invades tarsal plate or eyelid margin
  T3c Involves full thickness of eyelid
T4 Any eyelid tumour that invades adjacent ocular, or orbital, or facial structures
  T4a Tumour invades ocular or intraorbital structures
  T4b Tumour invades (or erodes through) the bony walls of orbit or extends to paranasal sinuses or invades the lacrimal sac/nasolacrimal duct or brain

N – Regional Lymph Nodes
NX Regional lymph nodes cannot be assessed
N0 No evidence of lymph node involvement
N1 Metastasis in a single ipsilateral regional lymph node, 3 cm or less in greatest dimension
N2 Metastasis in a single ipsilateral lymph node more than 3 cm in greatest dimension or in bilateral or contralateral lymph nodes

M – Distant Metastasis
M0 No distant metastasis
M1 Distant metastasis

pTNM Pathological Classification
The pT and pN categories correspond to the T and N categories. For pM see page 8.

Stage

<table>
<thead>
<tr>
<th>Stage</th>
<th>pT</th>
<th>pN</th>
<th>pM</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage 0</td>
<td>Tis</td>
<td>No</td>
<td>Mo</td>
</tr>
<tr>
<td>Stage IA</td>
<td>T1</td>
<td>No</td>
<td>Mo</td>
</tr>
<tr>
<td>Stage IB</td>
<td>T2a</td>
<td>No</td>
<td>Mo</td>
</tr>
<tr>
<td>Stage IIA</td>
<td>T2b, T2c, T3</td>
<td>No</td>
<td>Mo</td>
</tr>
<tr>
<td>Stage IIB</td>
<td>T4</td>
<td>No</td>
<td>Mo</td>
</tr>
<tr>
<td>Stage IIIA</td>
<td>Any T</td>
<td>N1</td>
<td>Mo</td>
</tr>
<tr>
<td>Stage IIIB</td>
<td>Any T</td>
<td>N2</td>
<td>Mo</td>
</tr>
<tr>
<td>Stage IV</td>
<td>Any T</td>
<td>Any N M1</td>
<td></td>
</tr>
</tbody>
</table>
# Prognostic Factor Grid – Eyelid

Prognostic factors for survival for eyelid cancers

<table>
<thead>
<tr>
<th>Prognostic factors</th>
<th>Tumour related</th>
<th>Host related</th>
<th>Environment related</th>
</tr>
</thead>
<tbody>
<tr>
<td>Essential</td>
<td>Location (worse prognosis if tumour involves the orbit or sinus)</td>
<td>Immunosuppression</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Perauricular and/or cervical lymph node involvement</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Systemic metastatic disease at presentation</td>
<td></td>
</tr>
<tr>
<td>Additional</td>
<td>BCC: nodular better than morpheaform type</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Sebaceous tumours have a worse prognosis than BCC or SCC</td>
<td></td>
<td></td>
</tr>
<tr>
<td>New and promising</td>
<td>Improvements in local control have been associated with less systemic recurrence</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>


# Malignant Melanoma of Skin

(ICD-O-3 C44, C51.0, C60.9, C63.2)

## Rules for Classification

There should be histological confirmation of the disease.

The following are the procedures for assessing N and M categories:

- **N categories**  
  Physical examination and imaging
- **M categories**  
  Physical examination and imaging

## Regional Lymph Nodes

The regional lymph nodes are those appropriate to the site of the primary tumour. See page 8.

## TNM Clinical Classification

**T – Primary Tumour**
The extent of the tumour is classified after excision, see pT, page 143.

**N – Regional Lymph Nodes**

NX Regional lymph nodes cannot be assessed
No No regional lymph node metastasis
N1 Metastasis in one regional lymph node or intralymphatic regional metastasis *without* nodal metastases
   N1a Only microscopic metastasis (clinically occult)
   N1b Macroscopic metastasis (clinically apparent)
   N1c Satellite or in transit metastasis *without* regional nodal metastasis
N2 Metastasis in two or three regional lymph nodes or intralymphatic regional metastasis *with* lymph node metastases
   N2a Only microscopic nodal metastasis
   N2b Macroscopic nodal metastasis
   N2c Satellite or in transit metastasis *with* only one regional nodal metastasis
N3 Metastasis in four or more regional lymph nodes, or matted metastatic regional lymph nodes, or satellite(s) or in transit metastasis *with* metastasis in two or more regional lymph node(s)
   N3a Only microscopic nodal metastasis
   N3b Macroscopic nodal metastasis
   N3c Satellite(s) or in transit metastasis with two or more regional nodal metastasis

**Note**

Satellites are tumour nests or nodules (macro. or microscopic) within 2 cm of the primary tumour. In transit metastasis involves skin or subcutaneous tissue more than 2 cm from the primary tumour but not beyond the regional lymph nodes.

**M – Distant Metastasis**

M0 No distant metastasis
M1 Distant metastasis*
   M1a Skin, subcutaneous tissue or lymph node(s) beyond the regional lymph nodes
   M1b Lung
   M1c Other non central nervous system sites
   M1d Central nervous system

**Notes**
Suffixes for M category:

(0) lactic dehydrogenase (LDH) – not elevated
(1) LDH – elevated

so that M1a(1) is metastasis in skin, subcutaneous tissue, or lymph node(s) beyond the regional lymph nodes with elevated LDH.

No suffix is used if LDH is not recorded or unspecified.

**pTNM Pathological Classification**

**pT – Primary Tumour**

pTX Primary tumour cannot be assessed
pTo No evidence of primary tumour
pTis Melanoma in situ (Clark level I) (atypical melanocytic hyperplasia, severe melanocytic dysplasia, not an invasive malignant lesion)

**Note**

* pTX includes shave biopsies and regressed melanomas.

pT1 Tumour 1 mm or less in thickness
   pT1a 0.8 mm or less in thickness without ulceration
   pT1b 0.8 mm in thickness with ulceration or more than 0.8 mm but no more than 1 mm in thickness, with or without ulceration

pT2 Tumour more than 1 mm but not more than 2 mm in thickness
   pT2a without ulceration
   pT2b with ulceration

pT3 Tumour more than 2 mm but not more than 4 mm in thickness
   pT3a without ulceration
   pT3b with ulceration

pT4 Tumour more than 4 mm in thickness
   pT4a without ulceration
   pT4b with ulceration

**pN – Regional Lymph Nodes**

The pN categories correspond to the N categories.

pNo Histological examination of a regional lymphadenectomy specimen will ordinarily include 6 or more lymph nodes. If the lymph nodes are negative, but the number
ordinarily examined is not met, classify as pNo. Classification based solely on sentinel node biopsy without subsequent axillary lymph node dissection is designated (sn) for sentinel node, e.g., (p)N1(sn). (See Introduction, page 7.)

pM – Distant Metastasis
For pM see page 8.

Clinical Stage

<table>
<thead>
<tr>
<th>Stage</th>
<th>pT</th>
<th>N</th>
<th>M</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Tis</td>
<td>No</td>
<td>Mo</td>
</tr>
<tr>
<td>IA</td>
<td>T1a</td>
<td>No</td>
<td>Mo</td>
</tr>
<tr>
<td>IB</td>
<td>T1b</td>
<td>No</td>
<td>Mo</td>
</tr>
<tr>
<td></td>
<td>T2a</td>
<td>No</td>
<td>Mo</td>
</tr>
<tr>
<td>IIA</td>
<td>T2b</td>
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<td>Mo</td>
</tr>
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<td>T3b</td>
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Pathological Stage*

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<th>N</th>
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<td>Mo</td>
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<td>I</td>
<td>T1</td>
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<td>Mo</td>
</tr>
<tr>
<td>IA</td>
<td>T1a</td>
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<td>Mo</td>
</tr>
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<td>Mo</td>
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<tr>
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<td>Any</td>
<td>N1, N2, N3</td>
<td>Mo</td>
</tr>
<tr>
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<td>T1a, T1b, T2a</td>
<td>N1a, N2a</td>
<td>Mo</td>
</tr>
<tr>
<td>IIIB</td>
<td>T1a, T1b, T2a</td>
<td>N1b, N1c, N2b</td>
<td>Mo</td>
</tr>
<tr>
<td></td>
<td>T2b−T3a</td>
<td>N1, N2a, N2b</td>
<td>Mo</td>
</tr>
</tbody>
</table>
Prognostic Factors Grid – Malignant Melanoma

Prognostic factors for melanoma

<table>
<thead>
<tr>
<th>Prognostic factors</th>
<th>Tumour related</th>
<th>Host related</th>
<th>Environment related</th>
</tr>
</thead>
<tbody>
<tr>
<td>Essential</td>
<td>Tumour thickness Mitotic rate Ulceration Extent of metastatic disease</td>
<td>Lymphocyte infiltrate Regression</td>
<td>Medications, especially immunosuppressives</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Sun exposure History Tanning bed use</td>
</tr>
<tr>
<td>Additional</td>
<td>Lymphovascular Perineural</td>
<td>Site of primary, Family history Personal medical history, especially immunodeficiency Gender (female more favourable) Age (younger age more favourable)</td>
<td></td>
</tr>
<tr>
<td>New and promising</td>
<td>Molecular: mutational, gene expression, proteomics, miRNA</td>
<td>Immunogenetics Other characteristics of host immune response</td>
<td></td>
</tr>
</tbody>
</table>


Merkel Cell Carcinoma of Skin

(ICD-O-3 C44.0-9, C63.2)

Rules for Classification

The classification applies only to Merkel cell carcinomas. There should be histological
confirmation of the disease.
The following are the procedures for assessing T, N, and M categories:

\[
\begin{align*}
T categories & \quad \text{Physical examination} \\
N categories & \quad \text{Physical examination and imaging} \\
M categories & \quad \text{Physical examination and imaging}
\end{align*}
\]

**Regional Lymph Nodes**

The regional lymph nodes are those appropriate to the site of the primary tumour. See page 8.

**TNM Clinical Classification**

**T – Primary Tumour**

- TX Primary tumour cannot be assessed
- T0 No evidence of primary tumour
- Tis Carcinoma in situ

T1 Tumour 2 cm or less in greatest dimension
T2 Tumour more than 2 cm but not more than 5 cm in greatest dimension
T3 Tumour more than 5 cm in greatest dimension
T4 Tumour invades deep extradermal structures, i.e., cartilage, skeletal muscle, fascia or bone

**N – Regional Lymph Nodes**

- NX Regional lymph nodes cannot be assessed
- N0 No regional lymph node metastasis
- N1 Regional lymph node metastasis
- N2 In transit metastasis *without* lymph node metastasis
- N3 In transit metastasis *with* lymph node metastasis

**Note**

In transit metastasis: a discontinuous tumour distinct from the primary lesion and located between the primary lesion and the draining regional lymph nodes or distal to the primary lesion.

**M – Distant Metastasis**

- Mo No distant metastasis
M1 Distant metastasis
  M1a Skin, subcutaneous tissues or non-regional lymph node(s)
  M1b Lung
  M1c Other site(s)

pTNM Pathological Classification

The pT category corresponds to the T category. For pM see page 8.

pNo Histological examination of a regional lymphadenectomy specimen will ordinarily include 6 or more lymph nodes. If the lymph nodes are negative, but the number ordinarily examined is not met, classify as pNo.

pNX Regional lymph nodes cannot be assessed

pNo No regional lymph node metastasis

pN1 Regional lymph node metastasis
  pN1a (sn)Microscopic metastasis detected on sentinel node biopsy
  pN1a Microscopic metastasis detected on node dissection
  pN1b Macroscopic metastasis (clinically apparent)

pN2 In-transit metastasis without lymph node metastasis

pN3 In-transit metastasis with lymph node metastasis

Note

In-transit metastasis: a discontinuous tumour distinct from the primary lesion and located between the primary lesion and the draining regional lymph nodes or distal to the primary lesion.

Clinical Stage

<table>
<thead>
<tr>
<th>Stage</th>
<th>Tis</th>
<th>No</th>
<th>Mo</th>
</tr>
</thead>
<tbody>
<tr>
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<td>Tis</td>
<td>No</td>
<td>Mo</td>
</tr>
<tr>
<td>Stage I</td>
<td>T1</td>
<td>No</td>
<td>Mo</td>
</tr>
<tr>
<td>Stage IIA</td>
<td>T2, T3</td>
<td>No</td>
<td>Mo</td>
</tr>
<tr>
<td>Stage IIB</td>
<td>T4</td>
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</tr>
<tr>
<td>Stage III</td>
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<td>N1, N2, N3</td>
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Pathological Stage

<table>
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<th>Stage</th>
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</tr>
</thead>
<tbody>
<tr>
<td>Stage 0</td>
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<td>Mo</td>
</tr>
<tr>
<td>Stage I</td>
<td>T1</td>
<td>No</td>
<td>Mo</td>
</tr>
<tr>
<td>Stage</td>
<td>T</td>
<td>N</td>
<td>M</td>
</tr>
<tr>
<td>---------</td>
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</tr>
<tr>
<td>IIA</td>
<td>T2, T3</td>
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<td>Mo</td>
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<tr>
<td>IIB</td>
<td>T4</td>
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<td>Mo</td>
</tr>
<tr>
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<td>T0</td>
<td>N1b</td>
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<td>N1b, N2, N3</td>
<td>Mo</td>
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<tr>
<td>IV</td>
<td>Any T</td>
<td>Any N</td>
<td>M1</td>
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</tbody>
</table>
Breast Tumours
(ICD-0-3 C50)

Introductory Notes
The site is described under the following headings:

- Rules for classification with the procedures for assessing T, N, and M categories; additional methods may be used when they enhance the accuracy of appraisal before treatment
- Anatomical subsites
- Definition of the regional lymph nodes
- TNM clinical classification
- pTNM pathological classification
- G histopathological grading
- Stage
- Prognostic grid

Rules for Classification
The classification applies only to carcinomas and concerns the male as well as the female breast. There should be histological confirmation of the disease. The anatomical subsite of origin should be recorded but is not considered in classification.

In the case of multiple simultaneous primary tumours in one breast, the tumour with the highest T category should be used for classification. Simultaneous bilateral breast cancers should be classified independently to permit division of cases by histological type.

The following are the procedures for assessing T, N, and M categories:

- **T categories**  Physical examination and imaging, e.g., mammography
- **N categories**  Physical examination and imaging
- **M categories**  Physical examination and imaging

Anatomical Subsites
1. Nipple (C50.0)
2. Central portion (C50.1)
3. Upper inner quadrant (C50.2)
4. Lower inner quadrant (C50.3)
5. Upper outer quadrant (C50.4)
6. Lower outer quadrant (C50.5)
7. Axillary tail (C50.6)

Regional Lymph Nodes

The regional lymph nodes are:

1. Axillary (ipsilateral): interpectoral (Rotter) nodes and lymph nodes along the axillary vein and its tributaries, which may be divided into the following levels:
   a. Level I (low axilla): lymph nodes lateral to the lateral border of pectoralis minor muscle
   b. Level II (mid axilla): lymph nodes between the medial and lateral borders of the pectoralis minor muscle and the interpectoral (Rotter) lymph nodes
   c. Level III (apical axilla): apical lymph nodes and those medial to the medial margin of the pectoralis minor muscle, excluding those designated as subclavicular or infraclavicular
2. Infraclavicular (subclavicular) (ipsilateral)
3. Internal mammary (ipsilateral): lymph nodes in the intercostal spaces along the edge of the sternum in the endothoracic fascia
4. Supraclavicular (ipsilateral)

Note

Intramammary lymph nodes are coded as axillary lymph nodes level I. Any other lymph node metastasis is coded as a distant metastasis (M1), including cervical or contralateral internal mammary lymph nodes.

TNM Clinical Classification

T – Primary Tumour

TX Primary tumour cannot be assessed
T0 No evidence of primary tumour
Tis Carcinoma in situ
Tis Ductal carcinoma in situ (DCIS)
Tis Lobular carcinoma in situ^a (LCIS)
Paget disease of the nipple not associated with invasive carcinoma and/or (Paget) carcinoma in situ (DCIS and/or LCIS) in the underlying breast parenchyma. Carcinomas in the breast parenchyma associated with Paget disease are categorized based on the size and characteristics of the parenchymal disease, although the presence of Paget disease should still be noted.

T1  Tumour 2 cm or less in greatest dimension
   T1mi Microinvasion 0.1 cm or less in greatest dimension\textsuperscript{b}
   T1a More than 0.1 cm but not more than 0.5 cm in greatest dimension
   T1b More than 0.5 cm but not more than 1 cm in greatest dimension
   T1c More than 1 cm but not more than 2 cm in greatest dimension
T2  Tumour more than 2 cm but not more than 5 cm in greatest dimension
T3  Tumour more than 5 cm in greatest dimension
T4  Tumour of any size with direct extension to chest wall and/or to skin (ulceration or skin nodules)\textsuperscript{c}
   T4a Extension to chest wall (does not include pectoralis muscle invasion only)
   T4b Ulceration, ipsilateral satellite skin nodules, or skin oedema (including peau d'orange)
   T4c Both 4a and 4b
T4d Inflammatory carcinoma\textsuperscript{d}

\textbf{Note}
\textsuperscript{a} The AJCC exclude Tis (LCIS).
\textsuperscript{b} Microinvasion is the extension of cancer cells beyond the basement membrane into the adjacent tissues with no focus more than 0.1 cm in greatest dimension. When there are multiple foci of microinvasion, the size of only the largest focus is used to classify the microinvasion. (Do not use the sum of all individual foci.) The presence of multiple foci of microinvasion should be noted, as it is with multiple larger invasive carcinomas.
\textsuperscript{c} Invasion of the dermis alone does not qualify as T4. Chest wall includes ribs, intercostal muscles, and serratus anterior muscle but not pectoral muscle.
\textsuperscript{d} Inflammatory carcinoma of the breast is characterized by diffuse, brawny induration of the skin with an erysipeloid edge, usually with no underlying mass. If the skin biopsy is negative and there is no localized measurable primary cancer, the T category is pTX when pathologically staging a clinical inflammatory carcinoma (T4d). Dimpling of the skin, nipple retraction, or other skin changes, except those in T4b and T4d, may occur in T1, T2, or T3 without affecting the classification.
N – Regional Lymph Nodes

NX Regional lymph nodes cannot be assessed (e.g., previously removed)
N0 No regional lymph node metastasis
N1 Metastasis in movable ipsilateral level I, II axillary lymph node(s)
N2 Metastasis in ipsilateral level I, II axillary lymph node(s) that are clinically fixed or matted; or in clinically detected* ipsilateral internal mammary lymph node(s) in the absence of clinically evident axillary lymph node metastasis
N2a Metastasis in axillary lymph node(s) fixed to one another (matted) or to other structures
N2b Metastasis only in clinically detected* internal mammary lymph node(s) and in the absence of clinically detected axillary lymph node metastasis
N3 Metastasis in ipsilateral infraclavicular (level III axillary) lymph node(s) with or without level I, II axillary lymph node involvement; or in clinically detected* ipsilateral internal mammary lymph node(s) with clinically evident level I, II axillary lymph node metastasis; or metastasis in ipsilateral supraclavicular lymph node(s) with or without axillary or internal mammary lymph node involvement
N3a Metastasis in infraclavicular lymph node(s)
N3b Metastasis in internal mammary and axillary lymph nodes
N3c Metastasis in supraclavicular lymph node(s)

Note
* Clinically detected is defined as detected by clinical examination or by imaging studies (excluding lymphoscintigraphy) and having characteristics highly suspicious for malignancy or a presumed pathological macrometastasis based on fine needle aspiration biopsy with cytological examination. Confirmation of clinically detected metastatic disease by fine needle aspiration without excision biopsy is designated with a (f) suffix, e.g. cN3a(f).

Excisional biopsy of a lymph node or biopsy of a sentinel node, in the absence of assignment of a pT, is classified as a clinical N, e.g., cN1. Pathological classification (pN) is used for excision or sentinel lymph node biopsy only in conjunction with a pathological T assignment.

M – Distant Metastasis

M0 No distant metastasis
M1 Distant metastasis

pTNM Pathological Classification
**pT – Primary Tumour**

The pathological classification requires the examination of the primary carcinoma with no gross tumour at the margins of resection. A case can be classified pT if there is only microscopic tumour in a margin. The pT categories correspond to the T categories.

**Note**

When classifying pT the tumour size is a measurement of the invasive component. If there is a large in situ component (e.g., 4 cm) and a small invasive component (e.g., 0.5 cm), the tumour is coded pT1a.

**pN – Regional Lymph Nodes**

The pathological classification requires the resection and examination of at least the low axillary lymph nodes (level I) (see page 152). Such a resection will ordinarily include 6 or more lymph nodes. If the lymph nodes are negative, but the number ordinarily examined is not met, classify as pN0.

- **pNX** Regional lymph nodes cannot be assessed (e.g., previously removed, or not removed for pathological study)
- **pN0** No regional lymph node metastasis*

**Note**

* Isolated tumour cell clusters (ITC) are single tumour cells or small clusters of cells not more than 0.2 mm in greatest extent that can be detected by routine H and E stains or immunohistochemistry. An additional criterion has been proposed to include a cluster of fewer than 200 cells in a single histological cross section. Nodes containing only ITCs are excluded from the total positive node count for purposes of N classification and should be included in the total number of nodes evaluated. (See Introduction, page 7.)

- **pN1** Micrometastases; or metastases in 1 to 3 axillary ipsilateral lymph nodes; and/or in internal mammary nodes with metastases detected by sentinel lymph node biopsy but not clinically detected*
  - **pN1mi** Micrometastases (larger than 0.2 mm and/or more than 200 cells, but none larger than 2.0 mm)
  - **pN1a** Metastasis in 1–3 axillary lymph node(s), including at least one larger than 2.0 mm in greatest dimension
  - **pN1b** Internal mammary lymph nodes
  - **pN1c** Metastasis in 1–3 axillary lymph nodes and internal mammary lymph nodes.
**pN2** Metastasis in 4–9 ipsilateral axillary lymph nodes, or in clinically detected* ipsilateral internal mammary lymph node(s) in the absence of axillary lymph node metastasis

**pN2a** Metastasis in 4–9 axillary lymph nodes, including at least one that is larger than 2.mm

**pN2b** Metastasis in clinically detected internal mammary lymph node(s), in the *absence* of axillary lymph node metastasis

**pN3**

**pN3a** Metastasis in 10 or more ipsilateral axillary lymph nodes (at least one larger than 2.mm) *or* metastasis in infraclavicular lymph nodes

**pN3b** Metastasis in clinically detected* internal ipsilateral mammary lymph node(s) in the *presence* of positive axillary lymph node(s); *or* metastasis in more than 3 axillary lymph nodes *and* in internal mammary lymph nodes with microscopic or macroscopic metastasis detected by sentinel lymph node biopsy but not clinically detected

**pN3c** Metastasis in ipsilateral supraclavicular lymph node(s)

**Post-treatment ypN:**

- Post-treatment yp ‘N’ should be evaluated as for clinical (pretreatment) ‘N’ methods (see Section N – Regional Lymph Nodes). The modifier ‘sn’ is used only if a sentinel node evaluation was performed after treatment. If no subscript is attached, it is assumed the axillary nodal evaluation was by axillary node dissection.
- The X classification will be used (ypNX) if no yp post-treatment SN or axillary dissection was performed
- N categories are the same as those used for pN.

**Notes**

* Clinically detected is defined as detected by imaging studies (excluding lymphoscintigraphy) or by clinical examination and having characteristics highly suspicious for malignancy or a presumed pathological macrometastasis based on fine needle aspiration biopsy with cytological examination.

Not clinically detected is defined as not detected by imaging studies (excluding lymphoscintigraphy) or not detected by clinical examination.

**pM – Distant Metastasis**

For pM see page 8.

**G Histopathological Grading**
For histopathological grading of invasive carcinoma the Nottingham Histological Score is recommended.\(^1\)

**Stage\(^a\)**

<table>
<thead>
<tr>
<th>Stage</th>
<th>T Status</th>
<th>N Status</th>
<th>M Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage 0</td>
<td>Tis</td>
<td>No</td>
<td>Mo</td>
</tr>
<tr>
<td>Stage IA</td>
<td>T1(^b)</td>
<td>No</td>
<td>Mo</td>
</tr>
<tr>
<td>Stage IB</td>
<td>T0, T1</td>
<td>N(1)mi</td>
<td>Mo</td>
</tr>
<tr>
<td>Stage IIA</td>
<td>T0, T1</td>
<td>N(1)</td>
<td>Mo</td>
</tr>
<tr>
<td></td>
<td>T2</td>
<td>No</td>
<td>Mo</td>
</tr>
<tr>
<td>Stage IIB</td>
<td>T2</td>
<td>N(1)</td>
<td>Mo</td>
</tr>
<tr>
<td></td>
<td>T3</td>
<td>No</td>
<td>Mo</td>
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<td>Mo</td>
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<td></td>
<td>T3</td>
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<td>Stage IIIB</td>
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<tr>
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<td>Any T</td>
<td>N3</td>
<td>Mo</td>
</tr>
<tr>
<td>Stage IV</td>
<td>Any T</td>
<td>Any N</td>
<td>M1</td>
</tr>
</tbody>
</table>

**Notes**

\(^a\) The AJCC also publish a prognostic group for breast tumours.

\(^b\) T1 includes T\(1\)mi.

**Prognostic Factors Grid – Breast**
<table>
<thead>
<tr>
<th>Prognostic factors</th>
<th>Tumour related</th>
<th>Host related</th>
<th>Environment related</th>
</tr>
</thead>
<tbody>
<tr>
<td>Essential</td>
<td>ER HER2 receptor Histological grade Number and percentage of involved nodes Tumour size Presence of lymphatic or vascular invasion (LVI+) Surgical resection margin status</td>
<td>Age Menopausal status</td>
<td>Prior radiation involving the chest or mediastinum (e.g. for Hodgkin disease)</td>
</tr>
<tr>
<td>Additional</td>
<td>Progesterone receptor Tumour profiling UPA, PAI.1</td>
<td>BRCA1 or 2 mutation Obesity</td>
<td>Use of postmenopausal hormone replacement therapy</td>
</tr>
<tr>
<td>New and promising</td>
<td>Ki.67</td>
<td>Level of activity or exercise Single nucleotide polymorphisms (SNPs) associated with drug metabolism or action</td>
<td></td>
</tr>
</tbody>
</table>


Reference

Introductory Notes

The following sites are included:

- Vulva
- Vagina
- Cervix uteri
- Corpus uteri
  - Endometrium
  - Uterine sarcomas
- Ovary, fallopian tube and primary peritoneal carcinoma
- Gestational trophoblastic tumours

Cervix uteri and corpus uteri were among the first sites to be classified by the TNM system. Originally, carcinoma of the cervix uteri was staged following the rules suggested by the Radiological Sub-Commission of the Cancer Commission of the Health Organization of The League of Nations. These rules were then adopted, with minor modifications, by the newly formed Fédération Internationale de Gynécologie et d'Obstétrique (FIGO). Finally, UICC brought them into the TNM in order to correspond to the FIGO stages. FIGO, UICC, and AJCC work in close collaboration in the revision process. The classification of tumours of ovary and fallopian tube has been revised in line with the recent FIGO update.¹

Each site is described under the following headings:

- Rules for classification with the procedures for assessing T, N, and M categories; additional methods may be used when they enhance the accuracy of appraisal before treatment
- Anatomical subsites where appropriate
- Definition of the regional lymph nodes
- TNM clinical classification
- pTNM pathological classification
- Stage
- Prognostic grid

Histopathological Grading
The definitions of the G categories apply to all carcinomas. These are:

**G – Histopathological Grading**

GX Grade of differentiation cannot be assessed  
G1 Well differentiated  
G2 Moderately differentiated  
G3 Poorly differentiated or undifferentiated

**Reference**


**Vulva**

(ICD-O-3 C51)
The definitions of the T, N, and M categories correspond to the FIGO stages.

**Rules for Classification**
The classification applies only to primary carcinomas of the vulva. There should be histological confirmation of the disease.

A carcinoma of the vulva that has extended to the vagina is classified as carcinoma of the vulva.

The following are the procedures for assessing T, N, and M categories:

- **T categories** Physical examination, endoscopy, and imaging  
- **N categories** Physical examination and imaging  
- **M categories** Physical examination and imaging

The FIGO stages are based on surgical staging. (TNM stages are based on clinical and/or pathological classification.)

**Regional Lymph Nodes**
The regional lymph nodes are the inguinofemoral (groin) nodes.

**TNM Clinical Classification**

**T – Primary tumour**

TX Primary tumour cannot be assessed
T0  No evidence of primary tumour

Tis  Carcinoma in situ (preinvasive carcinoma), intraepithelial neoplasia grade III (VIN III)

T1  Tumour confined to vulva or vulva and perineum
   T1a Tumour 2.0 cm or less in greatest dimension and with stromal invasion no greater than 1.0 mm\(^a\)
   T1b Tumour greater than 2.0 cm and or with stromal invasion greater than 1 mm\(^a\)

T2  Tumour invades any of the following structures: lower third urethra, lower third vagina, anus

T3\(^b\) Tumour invades any of the following perineal structures: upper 2/3 urethra, upper 2/3 vagina, bladder mucosa, rectal mucosa; or fixed to pelvic bone

Notes

\(^a\) The depth of invasion is defined as the measurement of the tumour from the epithelial–stromal junction of the adjacent most superficial dermal papilla to the deepest point of invasion.

\(^b\) T3 is not used by FIGO.

N – Regional Lymph Nodes

NX  Regional lymph nodes cannot be assessed
No  No regional lymph node metastasis
N1  Regional lymph node metastasis with the following features:
   N1a One or two lymph node metastasis each less than 5.0 mm
   N1b One lymph node metastases 5.0 mm or greater
N2  Regional lymph node metastasis with the following features:
   N2a Three or more lymph node metastases each less than 5.0 mm
   N2b Two or more lymph node metastases 5.0 mm or greater
   N2c Lymph node metastasis with extracapsular spread
N3  Fixed or ulcerated regional lymph node metastasis

M – Distant Metastasis

M0  No distant metastasis
M1  Distant metastasis (including pelvic lymph node metastasis)

pTNM Pathological Classification
The pT and pN categories correspond to the T and N categories. For pM see page 8.

pN0  Histological examination of an inguinofemoral lymphadenectomy specimen will ordinarily include 6 or more lymph nodes. If the lymph nodes are negative, but the number ordinarily examined is not met, classify as pN0.

Stage

<table>
<thead>
<tr>
<th>Stage</th>
<th>Tis</th>
<th>No</th>
<th>Mo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage 0</td>
<td>Tis</td>
<td>No</td>
<td>Mo</td>
</tr>
<tr>
<td>Stage I</td>
<td>T1</td>
<td>No</td>
<td>Mo</td>
</tr>
<tr>
<td>Stage IA</td>
<td>T1a</td>
<td>No</td>
<td>Mo</td>
</tr>
<tr>
<td>Stage IB</td>
<td>T1b</td>
<td>No</td>
<td>Mo</td>
</tr>
<tr>
<td>Stage II</td>
<td>T2</td>
<td>No</td>
<td>Mo</td>
</tr>
<tr>
<td>Stage IIIA</td>
<td>T1, T2</td>
<td>N1a, N1b</td>
<td>Mo</td>
</tr>
<tr>
<td>Stage IIIB</td>
<td>T1, T2</td>
<td>N2a, N2b</td>
<td>Mo</td>
</tr>
<tr>
<td>Stage IIIC</td>
<td>T1, T2</td>
<td>N2c</td>
<td>Mo</td>
</tr>
<tr>
<td>Stage IVA</td>
<td>T1, T2</td>
<td>N3</td>
<td>Mo</td>
</tr>
<tr>
<td></td>
<td>T3</td>
<td>Any N</td>
<td>Mo</td>
</tr>
<tr>
<td>Stage IVB</td>
<td>Any T</td>
<td>Any N</td>
<td>M1</td>
</tr>
</tbody>
</table>

Prognostic Factors Grid – Vulva
Prognostic risk factors for cancer of the vulva

<table>
<thead>
<tr>
<th>Prognostic factors</th>
<th>Tumour related</th>
<th>Host related</th>
<th>Environment related</th>
</tr>
</thead>
<tbody>
<tr>
<td>Essential</td>
<td>Lymph node metastases:</td>
<td></td>
<td>Experience of treating centre/concentration of care for</td>
</tr>
<tr>
<td></td>
<td>• Number</td>
<td></td>
<td>vulvar cancer patients in tertiary referral centres</td>
</tr>
<tr>
<td></td>
<td>• Size</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Extracapsular tumour</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>growth</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Additional</td>
<td>FIGO stage</td>
<td>Age</td>
<td>Surgical margins</td>
</tr>
<tr>
<td></td>
<td>Depth of invasion</td>
<td>Smoking</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Diameter of primary tumour</td>
<td>Adjacent dermatosis</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Histological type</td>
<td>(LS, VIN) Immune status</td>
<td></td>
</tr>
<tr>
<td>New and promising</td>
<td>EGFR status</td>
<td>HPV status</td>
<td></td>
</tr>
<tr>
<td></td>
<td>p53 over expression P16INK4a</td>
<td>Pretreatment haemoglobin</td>
<td></td>
</tr>
<tr>
<td></td>
<td>level Microvessel density</td>
<td>level</td>
<td></td>
</tr>
</tbody>
</table>


Vagina

(ICD-O-3 C52)

The definitions of the T and M categories correspond to the FIGO stages. Both systems are included for comparison.

Rules for Classification

The classification applies to primary carcinomas only. Tumours present in the vagina as secondary growths from either genital or extragenital sites are excluded. A tumour that has extended to the portio and reached the external os (orifice of uterus) is classified as carcinoma of the cervix. A vaginal carcinoma occurring 5 years after successful treatment (complete response) of a carcinoma of the cervix uteri is considered a primary vaginal carcinoma. A tumour involving the vulva is classified as carcinoma of the vulva. There should be histological confirmation of the disease.

The following are the procedures for assessing T, N, and M categories:

\[ T \text{ categories} \quad \text{Physical examination, endoscopy, and imaging} \]
The FIGO stages are based on surgical staging. (TNM stages are based on clinical and/or pathological classification.)

**Regional Lymph Nodes**

*Upper two thirds of vagina:* the pelvic nodes including obturator, internal iliac (hypogastric), external iliac, and pelvic nodes, NOS.

*Lower third of vagina:* the inguinal and femoral nodes.

**TNM Clinical Classification**

**T – Primary Tumour**

<table>
<thead>
<tr>
<th>TNM Categories</th>
<th>FIGO Stages</th>
<th>Definition</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>TX</td>
<td>Primary tumour cannot be assessed</td>
<td></td>
<td></td>
</tr>
<tr>
<td>T0</td>
<td>No evidence of primary tumour</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tis</td>
<td>Carcinoma in situ (preinvasive carcinoma)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>T1</td>
<td>I Tumour confined to vagina</td>
<td></td>
<td></td>
</tr>
<tr>
<td>T2</td>
<td>II Tumour invades paravaginal tissues (paracolpium)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>T3</td>
<td>III Tumour extends to pelvic wall</td>
<td></td>
<td></td>
</tr>
<tr>
<td>T4</td>
<td>IVA Tumour invades <em>mucosa</em> of bladder or rectum, or extends beyond the true pelvis*</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**M1** IVB Distant metastasis

**Note**

* The presence of bullous oedema is not sufficient evidence to classify a tumour as T4.

**N – Regional Lymph Nodes**

NX Regional lymph nodes cannot be assessed

N0 No regional lymph node metastasis

N1 Regional lymph node metastasis

**M – Distant Metastasis**

M0 No distant metastasis

M1 Distant metastasis
TNM Pathological Classification

The pT and pN categories correspond to the T and N categories. For pM see page 8.

pN0  Histological examination of an inguinal lymphadenectomy specimen will ordinarily include 6 or more lymph nodes; a pelvic lymphadenectomy specimen will ordinarily include 10 or more lymph nodes. If the lymph nodes are negative, but the number ordinarily examined is not met, classify as pN0.

Stage

<table>
<thead>
<tr>
<th>Stage</th>
<th>T</th>
<th>N</th>
<th>M</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage 0</td>
<td>Tis</td>
<td>No</td>
<td>Mo</td>
</tr>
<tr>
<td>Stage I</td>
<td>T1</td>
<td>No</td>
<td>Mo</td>
</tr>
<tr>
<td>Stage II</td>
<td>T2</td>
<td>No</td>
<td>Mo</td>
</tr>
<tr>
<td>Stage III</td>
<td>T3</td>
<td>No</td>
<td>Mo</td>
</tr>
<tr>
<td></td>
<td>T1, T2, T3</td>
<td>N1</td>
<td>Mo</td>
</tr>
<tr>
<td>Stage IVA</td>
<td>T4</td>
<td>Any N</td>
<td>Mo</td>
</tr>
<tr>
<td>Stage IVB</td>
<td>Any T</td>
<td>Any N</td>
<td>M1</td>
</tr>
</tbody>
</table>

Cervix Uteri

(ICD-O C53)

The definitions of the T and M categories correspond to the FIGO stages. Both systems are included for comparison.

Rules for Classification

The classification applies only to carcinomas. There should be histological confirmation of the disease.

The following are the procedures for assessing T, N, and M categories:

- **T categories**  Clinical examination and imaging*
- **N categories**  Clinical examination and imaging
- **M categories**  Clinical examination and imaging

Note

* The use of diagnostic imaging techniques to assess the size of the primary tumour is encouraged but is not mandatory. Other investigations, e.g., examination under anaesthesia, cystoscopy, sigmoidoscopy, intravenous pyelography, are optional and no longer mandatory.

The FIGO stages are based on clinical staging. For some Stage I subdivisions (IA–IB1) are
mainly pathological, including the histological examination of the cervix. (TNM stages are based on clinical and/or pathological classification.)

**Anatomical Subsites**

1. Endocervix (C53.0)
2. Exocervix (C53.1)

**Regional Lymph Nodes**

The regional lymph nodes are the paracervical, parametrial, hypogastric (internal iliac, obturator), common and external iliac, presacral, and lateral sacral nodes. Para-aortic nodes are not regional.

**TNM Clinical Classification**

**T – Primary Tumour**

<table>
<thead>
<tr>
<th>TNM Categories</th>
<th>FIGO Stages</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>TX</td>
<td></td>
<td>Primary tumour cannot be assessed</td>
</tr>
<tr>
<td>T0</td>
<td></td>
<td>No evidence of primary tumour</td>
</tr>
<tr>
<td>Tis</td>
<td></td>
<td>Carcinoma in situ (preinvasive carcinoma)</td>
</tr>
<tr>
<td>T1</td>
<td>I</td>
<td>Tumour confined to the cervix&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>T1a</td>
<td>IA</td>
<td>Invasive carcinoma diagnosed only by microscopy. Stromal invasion with a maximal depth of 5.0 mm measured from the base of the epithelium and a horizontal spread of 7.0 mm or less&lt;sup&gt;d&lt;/sup&gt;</td>
</tr>
<tr>
<td>T1a1</td>
<td>IA1</td>
<td>Measured stromal invasion 3.0 mm or less in depth and 7.0 mm or less in horizontal spread</td>
</tr>
<tr>
<td>T1a2</td>
<td>IA2</td>
<td>Measured stromal invasion more than 3.0 mm and not more than 5.0 mm with a horizontal spread of 7.0 mm or less</td>
</tr>
<tr>
<td>T1b</td>
<td>IB</td>
<td>Clinically visible lesion confined to the cervix or microscopic lesion greater than T1a/IA2</td>
</tr>
<tr>
<td>T1b1</td>
<td>IB1</td>
<td>Clinically visible lesion 4.0 cm or less in greatest dimension</td>
</tr>
<tr>
<td>T1b2</td>
<td>IB2</td>
<td>Clinically visible lesion more than 4.0 cm in greatest dimension</td>
</tr>
<tr>
<td>T2</td>
<td>II</td>
<td>Tumour invades beyond uterus but not to pelvic wall or to lower third of vagina</td>
</tr>
<tr>
<td>T2a</td>
<td>IIA</td>
<td>Tumour without parametrial invasion</td>
</tr>
<tr>
<td>T2a1</td>
<td>IIA1</td>
<td>Clinically visible lesion 4.0 cm or less in greatest dimension</td>
</tr>
<tr>
<td>T2a2</td>
<td>IIA2</td>
<td>Clinically visible lesion more than 4.0 cm in greatest dimension</td>
</tr>
<tr>
<td>T2b</td>
<td>IIB</td>
<td>Tumour with parametrial invasion</td>
</tr>
<tr>
<td>-----</td>
<td>-----</td>
<td>-------------------------------</td>
</tr>
<tr>
<td>T3</td>
<td>III</td>
<td>Tumour, involves lower third of vagina, or extends to pelvic wall, or causes hydronephrosis or non-functioning kidney</td>
</tr>
<tr>
<td>T3a</td>
<td>IIIA</td>
<td>Tumour involves lower third of vagina</td>
</tr>
<tr>
<td>T3b</td>
<td>IIIB</td>
<td>Tumour extends to pelvic wall, or causes hydronephrosis or non-functioning kidney</td>
</tr>
<tr>
<td>T4</td>
<td>IVA</td>
<td>Tumour invades mucosa of the bladder or rectum, or extends beyond true pelvis</td>
</tr>
</tbody>
</table>

**Notes**

a. Extension to corpus uteri should be disregarded.

b. The depth of invasion should be taken from the base of the epithelium, either surface or glandular, from which it originates. The depth of invasion is defined as the measurement of the tumour from the epithelial–stromal junction of the adjacent most superficial papillae to the deepest point of invasion. Vascular space involvement, venous or lymphatic, does not affect classification.

c. All macroscopically visible lesions even with superficial invasion are T1b/IB.

d. Vascular space involvement, venous or lymphatic, does not affect classification.

e. Bullous oedema is not sufficient to classify a tumour as T4.

**N – Regional lymph nodes**

NX Regional lymph nodes cannot be assessed  
No No regional lymph node metastasis  
N1 Regional lymph node metastasis

**Note**

* No FIGO equivalent.

**M – Distant Metastasis**

Mo No distant metastasis  
M1 Distant metastasis (includes inguinal lymph nodes and intraperitoneal disease). It excludes metastasis to vagina, pelvic serosa, and adnexa

**pTNM Pathological Classification**
The pT and pN categories correspond to the T and N categories. For pM see page 8.

pN0 Histological examination of a pelvic lymphadenectomy specimen will ordinarily include 10 or more lymph nodes. If the lymph nodes are negative, but the number ordinarily examined is not met, classify as pN0.

Stage

<table>
<thead>
<tr>
<th>Stage</th>
<th>T</th>
<th>N</th>
<th>M</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage 0</td>
<td>Tis</td>
<td>No</td>
<td>Mo</td>
</tr>
<tr>
<td>Stage I</td>
<td>T1</td>
<td>No</td>
<td>Mo</td>
</tr>
<tr>
<td>Stage IA</td>
<td>T1a</td>
<td>No</td>
<td>Mo</td>
</tr>
<tr>
<td>Stage IA1</td>
<td>T1a1</td>
<td>No</td>
<td>Mo</td>
</tr>
<tr>
<td>Stage IA2</td>
<td>T1a2</td>
<td>No</td>
<td>Mo</td>
</tr>
<tr>
<td>Stage IB</td>
<td>T1b</td>
<td>No</td>
<td>Mo</td>
</tr>
<tr>
<td>Stage IB1</td>
<td>T1b1</td>
<td>No</td>
<td>Mo</td>
</tr>
<tr>
<td>Stage IB2</td>
<td>T1b2</td>
<td>No</td>
<td>Mo</td>
</tr>
<tr>
<td>Stage II</td>
<td>T2</td>
<td>No</td>
<td>Mo</td>
</tr>
<tr>
<td>Stage IIA</td>
<td>T2a</td>
<td>No</td>
<td>Mo</td>
</tr>
<tr>
<td>Stage IIA1</td>
<td>T2a1</td>
<td>No</td>
<td>Mo</td>
</tr>
<tr>
<td>Stage IIA2</td>
<td>T2a2</td>
<td>No</td>
<td>Mo</td>
</tr>
<tr>
<td>Stage IIB</td>
<td>T2b</td>
<td>No</td>
<td>Mo</td>
</tr>
<tr>
<td>Stage III</td>
<td>T3</td>
<td>No</td>
<td>Mo</td>
</tr>
<tr>
<td>Stage IIIA</td>
<td>T3a</td>
<td>No</td>
<td>Mo</td>
</tr>
<tr>
<td>Stage IIIB</td>
<td>T3b</td>
<td>Any N</td>
<td>Mo</td>
</tr>
<tr>
<td></td>
<td></td>
<td>T1, T2, T3</td>
<td>N1, Mo</td>
</tr>
<tr>
<td>Stage IVA</td>
<td>T4</td>
<td>Any N</td>
<td>Mo</td>
</tr>
<tr>
<td>Stage IVB</td>
<td>Any T</td>
<td>Any N</td>
<td>M1</td>
</tr>
</tbody>
</table>
**Prognostic risk factors in cervical cancer**

<table>
<thead>
<tr>
<th>Prognostic factors</th>
<th>Tumour related</th>
<th>Host related</th>
<th>Environment related</th>
</tr>
</thead>
<tbody>
<tr>
<td>Essential</td>
<td>Unilateral vs bilateral disease</td>
<td>Immunosuppression (i.e. HIV infection)</td>
<td>Quality of and availability of anticancer therapies</td>
</tr>
<tr>
<td></td>
<td>Parametrial invasion</td>
<td>Performance status</td>
<td>Expertise of healthcare personnel</td>
</tr>
<tr>
<td></td>
<td>Invasion to side wall</td>
<td>Morbid obesity</td>
<td>Multidisciplinary teams</td>
</tr>
<tr>
<td></td>
<td>Size of tumour</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Lymph node invasion</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Positive surgical margins</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Additional</td>
<td>Lymphovascular space invasion</td>
<td>Anaemia during treatment</td>
<td>Ability to manage co-morbid conditions</td>
</tr>
<tr>
<td></td>
<td>Histological type</td>
<td></td>
<td></td>
</tr>
<tr>
<td>New and promising</td>
<td>Tumour hypoxia VEGF, mEGFR, HIF1α, COX2 PAI1</td>
<td>Serum MyoDI hypermethylation</td>
<td>Adequate laboratory facilities to measure tumour markers</td>
</tr>
<tr>
<td></td>
<td>expression SCCAg and hsCRP for early detection of recurrence</td>
<td>Persistence of HPV infection following treatment</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>


**Uterus – Endometrium**

(ICD-O-3 C54.1, C55)

The definitions of the T, N, and M categories correspond to the FIGO stages. Both systems are included for comparison.

**Rules for Classification**

The classification applies to endometrial carcinomas and carcinosarcomas (malignant mixed mesodermal tumours). There should be histological verification with subdivision by histological type and grading of the carcinomas. The diagnosis should be based on examination of specimens taken by endometrial biopsy.

The following are the procedures for assessing T, N, and M categories:

- **T categories**  Physical examination and imaging including urography and cystoscopy
- **N categories**  Physical examination and imaging including urography
- **M categories**  Physical examination and imaging.

The FIGO stages are based on surgical staging. (TNM stages are based on clinical and/or pathological classification.)
Anatomical Subsites
1. Isthmus uteri (C54.0)
2. Fundus uteri (C54.3)
3. Endometrium (C54.1)

Regional Lymph Nodes
The regional lymph nodes are the pelvic (hypogastric [obturator, internal iliac], common and external iliac, parametrial, and sacral) and the paraaortic nodes.

TNM Clinical Classification

T – Primary Tumour

<table>
<thead>
<tr>
<th>TNM Categories</th>
<th>FIGO Stages</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>TX</td>
<td></td>
<td>Primary tumour cannot be assessed</td>
</tr>
<tr>
<td>To</td>
<td></td>
<td>No evidence of primary tumour</td>
</tr>
<tr>
<td>T1</td>
<td>IA&lt;sup&gt;a&lt;/sup&gt;</td>
<td>Tumour confined to the corpus uteri&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>T1a</td>
<td>IA&lt;sup&gt;a&lt;/sup&gt;</td>
<td>Tumour limited to endometrium or invading less than half of myometrium</td>
</tr>
<tr>
<td>T1b</td>
<td>IB</td>
<td>Tumour invades one half or more of myometrium</td>
</tr>
<tr>
<td>T2</td>
<td>II</td>
<td>Tumour invades cervical stroma, but does not extend beyond the uterus</td>
</tr>
<tr>
<td>T3</td>
<td>III</td>
<td>Local and/or regional spread as specified here:</td>
</tr>
<tr>
<td>T3a</td>
<td>IIIA</td>
<td>Tumour invades the serosa of the corpus uteri or adnexae (direct extension or metastasis)</td>
</tr>
<tr>
<td>T3b</td>
<td>IIIB</td>
<td>Vaginal or parametrial involvement (direct extension or metastasis)</td>
</tr>
<tr>
<td>N1,N2</td>
<td>IIIC</td>
<td>Metastasis to pelvic or paraaortic lymph nodes&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>N1</td>
<td>IIIC1</td>
<td>Metastasis to pelvic lymph nodes</td>
</tr>
<tr>
<td>N2</td>
<td>IIIC2</td>
<td>Metastasis to paraaortic lymph nodes with or without metastasis to pelvic lymph nodes</td>
</tr>
<tr>
<td>T4&lt;sup&gt;c&lt;/sup&gt;</td>
<td>IV</td>
<td>Tumour invades bladder/bowel mucosa</td>
</tr>
</tbody>
</table>

Notes
<sup>a</sup> Endocervical glandular involvement only should be considered as stage I.
Positive cytology has to be reported separately without changing the stage.

The presence of bullous oedema is not sufficient evidence to classify as T4.

N – Regional Lymph Nodes

NX Regional lymph nodes cannot be assessed
No No regional lymph node metastasis
N1 Regional lymph node metastasis to pelvic lymph nodes
N2 Regional lymph node metastasis to paraaortic lymph nodes with or without metastasis to pelvic lymph nodes

M – Distant Metastasis

Mo No distant metastasis
M1 Distant metastasis (excluding metastasis to vagina, pelvic serosa, or adnexa, including metastasis to inguinal lymph nodes, intra-abdominal lymph nodes other than paraaortic or pelvic nodes)

pTNM Pathological Classification

The pT and pN categories correspond to the T and N categories. For pM see page 8.
pN0 Histological examination of a pelvic lymphadenectomy specimen will ordinarily include 10 or more lymph nodes. If the lymph nodes are negative, but the number ordinarily examined is not met, classify as pN0.

G Histopathological Grading

For histopathological grading use G1, G2, or G3. For details see Creasman et al. 2006.

Stage

<table>
<thead>
<tr>
<th>Stage</th>
<th>pT</th>
<th>pN</th>
<th>pM</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage 0</td>
<td>Tis</td>
<td>No</td>
<td>Mo</td>
</tr>
<tr>
<td>Stage IA</td>
<td>T1a</td>
<td>No</td>
<td>Mo</td>
</tr>
<tr>
<td>Stage IB</td>
<td>T1b</td>
<td>No</td>
<td>Mo</td>
</tr>
<tr>
<td>Stage II</td>
<td>T2</td>
<td>No</td>
<td>Mo</td>
</tr>
<tr>
<td>Stage IIIA</td>
<td>T3a</td>
<td>No</td>
<td>Mo</td>
</tr>
<tr>
<td>Stage IIIB</td>
<td>T3b</td>
<td>No</td>
<td>Mo</td>
</tr>
<tr>
<td>Stage III</td>
<td>T1, T2, T3</td>
<td>N1, N2</td>
<td>Mo</td>
</tr>
<tr>
<td>Stage IIIC1</td>
<td>T1, T2, T3</td>
<td>N1</td>
<td>Mo</td>
</tr>
<tr>
<td>Stage IIIC2</td>
<td>T1, T2, T3</td>
<td>N2</td>
<td>Mo</td>
</tr>
</tbody>
</table>
Stage IVA  T4  Any N  Mo
Stage IVB  Any T  Any N  M1

Prognostic Grid – Endometrium

Prognostic factors for endometrial carcinoma

<table>
<thead>
<tr>
<th>Prognostic factors</th>
<th>Tumour related</th>
<th>Host related</th>
<th>Environment related</th>
</tr>
</thead>
</table>
| Essential          | Depth of myometrial invasion  
Grade of differentiation  
Tumour cell type  
Lymphovascular space invasion | Postsurgical treatment | |
| Additional         | Metastasis to lymph nodes  
Site of distant metastasis | Age  
Performance status  
Race Co. morbidities | Extent of resection  
Postsurgical treatment |
| New and promising  | Molecular profile | | |


Reference


Uterine Sarcomas

*(Leiomyosarcoma, Endometrial Stromal Sarcoma, Adenosarcoma)*  
*(ICD-O-3 53, 54)*

The definitions of the T, N, and M categories correspond to the FIGO stages. Both systems are included for comparison.\(^1,2\)

Rules for Classification

The classification applies to sarcomas except for carcinosarcoma, which is classified as carcinoma of the endometrium. There should be histological confirmation and division of cases by histological type.
The following are the procedures for assessing T, N, and M categories:

- **T categories**  Physical examination and imaging
- **N categories**  Physical examination and imaging
- **M categories**  Physical examination and imaging

The FIGO stages are based on surgical staging. (TNM stages are based on clinical and/or pathological classification.)

### Anatomical Subsites

1. Cervix uteri (C53)
2. Isthmus uteri (C54.0)
3. Fundus uteri (C54.3)

### Histological Types of Tumours

- Leiomyosarcoma  8890/3
- Endometrial stromal sarcoma  8930/3
- Adenosarcoma  8933/3

### Regional Lymph Nodes

The regional lymph nodes are the pelvic (hypogastric [obturateur, internal iliac], common and external iliac, parametrial, and sacral) and the para-aortic nodes.

### TNM Clinical Classification

**Leiomyosarcoma, Endometrial stromal sarcoma**

<table>
<thead>
<tr>
<th>TNM categories</th>
<th>FIGO Stage</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>T1</td>
<td>I</td>
<td>Tumour limited to the uterus</td>
</tr>
<tr>
<td>T1a</td>
<td>IA</td>
<td>Tumour 5 cm or less in greatest dimension</td>
</tr>
<tr>
<td>T1b</td>
<td>IB</td>
<td>Tumour more than 5 cm</td>
</tr>
<tr>
<td>T2</td>
<td>II</td>
<td>Tumour extends beyond the uterus, within the pelvis</td>
</tr>
<tr>
<td>T2a</td>
<td>IIA</td>
<td>Tumour involves adnexa</td>
</tr>
<tr>
<td>T2b</td>
<td>IIB</td>
<td>Tumour involves other pelvic tissues</td>
</tr>
<tr>
<td>T3</td>
<td>III</td>
<td>Tumour infiltrates abdominal tissues</td>
</tr>
<tr>
<td>T3a</td>
<td>IIIA</td>
<td>One site</td>
</tr>
<tr>
<td>T3b</td>
<td>IIIB</td>
<td>More than one site</td>
</tr>
</tbody>
</table>
**Note**

Simultaneous tumours of the uterine corpus and ovary/pelvis in association with ovarian/pelvic endometriosis should be classified as independent primary tumours.

**Adenosarcoma**

**T – Primary tumour**

<table>
<thead>
<tr>
<th>TNM categories</th>
<th>FIGO Stage</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>T1</td>
<td>I</td>
<td>Tumour limited to the uterus</td>
</tr>
<tr>
<td>T1a</td>
<td>IA</td>
<td>Tumour limited to the endometrium/endocervix</td>
</tr>
<tr>
<td>T1b</td>
<td>IB</td>
<td>Tumour invades to less than half of the myometrium</td>
</tr>
<tr>
<td>T1c</td>
<td>IC</td>
<td>Tumour invades more than half of the myometrium</td>
</tr>
<tr>
<td>T2</td>
<td>II</td>
<td>Tumour extends beyond the uterus, within the pelvis</td>
</tr>
<tr>
<td>T2a</td>
<td>IIA</td>
<td>Tumour involves adnexa</td>
</tr>
<tr>
<td>T2b</td>
<td>IIB</td>
<td>Tumour involves other pelvic tissues</td>
</tr>
<tr>
<td>T3</td>
<td>III</td>
<td>Tumour involves abdominal tissues</td>
</tr>
<tr>
<td>T3a</td>
<td>IIIA</td>
<td>One site</td>
</tr>
<tr>
<td>T3b</td>
<td>IIIB</td>
<td>More than one site</td>
</tr>
<tr>
<td>N1</td>
<td>IIIC</td>
<td>Metastasis to regional lymph nodes</td>
</tr>
<tr>
<td>T4</td>
<td>IVA</td>
<td>Tumour invades bladder or rectum</td>
</tr>
<tr>
<td>M1</td>
<td>IVB</td>
<td>Distant metastasis</td>
</tr>
</tbody>
</table>

**Note**

Simultaneous tumours of the uterine corpus and ovary/pelvis in association with ovarian/pelvic endometriosis should be classified as independent primary tumours.

**N – Regional Lymph Nodes**

- NX Regional lymph nodes cannot be assessed
- No No regional lymph node metastasis
- N1 Regional lymph node metastasis

**M – Distant Metastasis**
pTNM Pathological Classification

The pT and pN categories correspond to the T and N categories. For pM see page 8.

Stage – Uterine Sarcomas

<table>
<thead>
<tr>
<th>Stage</th>
<th>T</th>
<th>N</th>
<th>M</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage I</td>
<td>T1</td>
<td>No</td>
<td>Mo</td>
</tr>
<tr>
<td>Stage IA</td>
<td>T1a</td>
<td>No</td>
<td>Mo</td>
</tr>
<tr>
<td>Stage IB</td>
<td>T1b</td>
<td>No</td>
<td>Mo</td>
</tr>
<tr>
<td>Stage IC*</td>
<td>T1c</td>
<td>No</td>
<td>Mo</td>
</tr>
<tr>
<td>Stage II</td>
<td>T2</td>
<td>No</td>
<td>Mo</td>
</tr>
<tr>
<td>Stage IIA</td>
<td>T2a</td>
<td>No</td>
<td>Mo</td>
</tr>
<tr>
<td>Stage IIB</td>
<td>T2b</td>
<td>No</td>
<td>Mo</td>
</tr>
<tr>
<td>Stage IIIA</td>
<td>T3a</td>
<td>No</td>
<td>Mo</td>
</tr>
<tr>
<td>Stage IIIB</td>
<td>T3b</td>
<td>No</td>
<td>Mo</td>
</tr>
<tr>
<td>Stage IIIC</td>
<td>T1, T2, T3 N1</td>
<td>Mo</td>
<td></td>
</tr>
<tr>
<td>Stage IVA</td>
<td>T4</td>
<td>Any N</td>
<td>Mo</td>
</tr>
<tr>
<td>Stage IVB</td>
<td>Any T</td>
<td>Any N</td>
<td>Mo</td>
</tr>
</tbody>
</table>

Note

* Stage IC does not apply for leiomyosarcoma and endometrial stromal sarcoma.

References


Ovarian, Fallopian Tube, and Primary Peritoneal Carcinoma

(ICD-O-3 C56; ICD-O-3 C57)

The definitions of the T, N, and M categories correspond to the FIGO stages. Both systems are included for comparison.

Rules for Classification
The classification applies to malignant ovarian neoplasms of both epithelial and stromal origin including those of borderline malignancy or of low malignant potential corresponding to ‘common epithelial tumours’ of the earlier terminology.

The classification also applies to carcinoma of the fallopian tubes and to carcinomas of the peritoneum (Müllerian origin).

There should be histological confirmation of the disease and division of cases by histological type.

The following are the procedures for assessing T, N, and M categories:

**T categories**  
Clinical examination, imaging, surgical exploration (laparoscopy/laparotomy)

**N categories**  
Clinical examination, imaging, surgical exploration (laparoscopy/laparotomy)

**M categories**  
Clinical examination, imaging, surgical exploration (laparoscopy/laparotomy)

The FIGO stages are based on surgical staging. (TNM stages are based on clinical and/or pathological classification.)

### Regional Lymph Nodes

The regional lymph nodes are the hypogastric (obturator), common iliac, external iliac, lateral sacral, paraaortic, retroperitoneal, and inguinal nodes.

### TNM Clinical Classification

#### T – Primary Tumour

<table>
<thead>
<tr>
<th>TNM categories</th>
<th>FIGO Stage</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>TX</td>
<td></td>
<td>Primary tumour cannot be assessed</td>
</tr>
<tr>
<td>T0</td>
<td>I</td>
<td>No evidence of primary tumour</td>
</tr>
<tr>
<td>T1</td>
<td>IA</td>
<td>Tumour limited to the ovaries (one or both) or fallopian tube(s)</td>
</tr>
<tr>
<td>T1a</td>
<td>IA</td>
<td>Tumour limited to one ovary; capsule intact, no tumour on ovarian surface or fallopian tube surface; no malignant cells in ascites or peritoneal washings</td>
</tr>
<tr>
<td>T1b</td>
<td>IB</td>
<td>Tumour limited to both ovaries or fallopian tubes; capsule intact, no tumour on ovarian or fallopian tube surface; no malignant cells in ascites or peritoneal washings</td>
</tr>
<tr>
<td>T1c</td>
<td>IC</td>
<td>Tumour limited to one or both ovaries or fallopian tubes with...</td>
</tr>
<tr>
<td>Stage</td>
<td>Substage</td>
<td>Description</td>
</tr>
<tr>
<td>-------</td>
<td>----------</td>
<td>-------------</td>
</tr>
<tr>
<td>T1c1</td>
<td></td>
<td>Surgical spill</td>
</tr>
<tr>
<td>T1c2</td>
<td></td>
<td>Capsule ruptured before surgery or tumour on ovarian or fallopian tube surface</td>
</tr>
<tr>
<td>T1c3</td>
<td></td>
<td>Malignant cells in ascites or peritoneal washings</td>
</tr>
<tr>
<td>T2</td>
<td>II</td>
<td>Tumour involves one or both ovaries or fallopian tubes with pelvic extension (below the pelvic brim) or primary peritoneal cancer</td>
</tr>
<tr>
<td>T2a</td>
<td>IIA</td>
<td>Extension and/or implants on uterus and/or fallopian tube(s) and/or ovary(ies)</td>
</tr>
<tr>
<td>T2b</td>
<td>IIB</td>
<td>Extension to other pelvic tissues, including bowel within the pelvis</td>
</tr>
<tr>
<td>T3</td>
<td>IIIa</td>
<td>Tumour involves one or both ovaries or fallopian tubes or primary peritoneal carcinoma with cytologically or histologically confirmed spread to the peritoneum outside the pelvis and/or metastasis to the retroperitoneal lymph nodes</td>
</tr>
<tr>
<td>N1</td>
<td></td>
<td>Retroperitoneal lymph node metastasis only</td>
</tr>
<tr>
<td>N1a</td>
<td>IIIA1i</td>
<td>Lymph node metastasis not more than 10 mm in greatest dimension</td>
</tr>
<tr>
<td>N1b</td>
<td>IIIA1ii</td>
<td>Lymph node metastasis more than 10 mm in greatest dimension</td>
</tr>
<tr>
<td>T3a</td>
<td>IIIA2</td>
<td>Microscopic extrapelvic (above the pelvic brim) peritoneal involvement with or without retroperitoneal lymph node, including bowel involvement</td>
</tr>
<tr>
<td>T3b</td>
<td>IIIB</td>
<td>Macroscopic peritoneal metastasis beyond pelvic brim 2 cm, or less in greatest dimension, including bowel involvement outside the pelvis with or without retroperitoneal nodes</td>
</tr>
<tr>
<td>T3c</td>
<td>IIIC</td>
<td>Peritoneal metastasis beyond pelvic brim more than 2 cm in greatest dimension and/or retroperitoneal lymph node metastasis (includes extension of tumour to capsule of liver and spleen without parenchymal involvement of either organ)</td>
</tr>
<tr>
<td>M1</td>
<td>IV</td>
<td>Distant metastasis (excludes peritoneal metastasis)</td>
</tr>
<tr>
<td>M1a</td>
<td>IVA</td>
<td>Pleural effusion with positive cytology</td>
</tr>
<tr>
<td>M1b</td>
<td>IVB</td>
<td>Parenchymal metastasis and metastasis to extra-abdominal organs (including inguinal lymph nodes and lymph nodes outside the abdominal cavity)</td>
</tr>
</tbody>
</table>

Notes
Liver capsule metastasis is T3/stage III.
Liver parenchymal metastasis M1/stage IV.

N – Regional Lymph Nodes

NX Regional lymph nodes cannot be assessed
No No regional lymph node metastasis
N1 Regional lymph node metastasis
   N1 IIIA1 Retroperitoneal lymph node metastasis only
   N1a IIIA1i Lymph node metastasis no more than 10 mm in greatest dimension
   N1b IIIA1ii Lymph node metastasis more than 10 mm in greatest dimension

M – Distant Metastasis

M0 No distant metastasis
M1 Distant metastasis

pTNM Pathological Classification

The pT and pN categories correspond to the T and N categories. For pM see page 8.

pNo Histological examination of a pelvic lymphadenectomy specimen will ordinarily include 10 or more lymph nodes. If the lymph nodes are negative, but the number ordinarily examined is not met, classify as pNo.

Stage

<table>
<thead>
<tr>
<th>Stage</th>
<th>T</th>
<th>N</th>
<th>M</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>T1</td>
<td>No</td>
<td>Mo</td>
</tr>
<tr>
<td>IA</td>
<td>T1a</td>
<td>No</td>
<td>Mo</td>
</tr>
<tr>
<td>IB</td>
<td>T1b</td>
<td>No</td>
<td>Mo</td>
</tr>
<tr>
<td>IC</td>
<td>T1c</td>
<td>No</td>
<td>Mo</td>
</tr>
<tr>
<td>II</td>
<td>T2</td>
<td>No</td>
<td>Mo</td>
</tr>
<tr>
<td>IIA</td>
<td>T2a</td>
<td>No</td>
<td>Mo</td>
</tr>
<tr>
<td>IIB</td>
<td>T2b</td>
<td>No</td>
<td>Mo</td>
</tr>
<tr>
<td>IIC</td>
<td>T2c</td>
<td>No</td>
<td>Mo</td>
</tr>
<tr>
<td>IIIA1</td>
<td>T1/2</td>
<td>N1</td>
<td>Mo</td>
</tr>
<tr>
<td>IIIA2</td>
<td>T3a</td>
<td>No, N1</td>
<td>Mo</td>
</tr>
<tr>
<td>IIIB</td>
<td>T3b</td>
<td>No, N1</td>
<td>Mo</td>
</tr>
<tr>
<td>IIIC</td>
<td>T3c</td>
<td>No, N1</td>
<td>Mo</td>
</tr>
<tr>
<td>IV</td>
<td>Any T</td>
<td>Any N</td>
<td>M1</td>
</tr>
</tbody>
</table>
### Prognostic Factors Grid – Tumours of the Ovary, Fallopian Tube and Peritoneal Carcinoma

Prognostic risk factor for epithelial ovarian cancer

<table>
<thead>
<tr>
<th>Prognostic factors</th>
<th>Tumour related</th>
<th>Host related</th>
<th>Environment related</th>
</tr>
</thead>
<tbody>
<tr>
<td>Essential</td>
<td>Histological type Grade</td>
<td>Age Co. morbidities</td>
<td>Maximum diameter of residual disease after optimal debulking</td>
</tr>
<tr>
<td></td>
<td>Surgical stage Residual disease</td>
<td>Performance status</td>
<td></td>
</tr>
<tr>
<td>Additional</td>
<td>Nodal involvement Site of metastasis DNA ploidy</td>
<td><strong>BRCA 1</strong> Genetic predisposition</td>
<td>Type of chemotherapy</td>
</tr>
<tr>
<td></td>
<td>CA125</td>
<td></td>
<td>CA125 fall Ultra. radical surgery</td>
</tr>
<tr>
<td>New and promising</td>
<td>Molecular profile Cellular proliferative activity</td>
<td>Interval debulking surgery (IDS)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Tumour angiogenesis markers p53 expression</td>
<td></td>
<td>Neoadjuvant chemotherapy</td>
</tr>
<tr>
<td></td>
<td>of human kallikrein (hK) genes, particularly hKs</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>6 10 11</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>


### Reference


### Gestational Trophoblastic Neoplasms

*(ICD-O-3 C58)*

The following classification for gestational trophoblastic tumours is based on that of FIGO adopted in 1992 and updated in 2002. The definitions of T and M categories correspond to the FIGO stages. Both systems are included for comparison. In contrast to other sites, an N (regional lymph node) classification does not apply to these tumours. A prognostic scoring index, which is based on factors other than the anatomic extent of the
disease, is used to assign cases to high-risk and low-risk categories, and these categories are used in stage grouping.

**Rules for Classification**

The classification applies to choriocarcinoma (9100/3), invasive hydatidiform mole (9100/1), and placental site trophoblastic tumour (9104/1). Placental site tumours should be reported separately. Histological confirmation is not required if the human chorionic gonadotropin (βhCG) level is abnormally elevated. History of prior chemotherapy for this disease should be noted.

The following are the procedures for assessing T and M categories:

- **T categories:** Clinical examination, imaging and endoscopy, and serum/urine βhCG level
- **M categories:** Clinical examination, imaging, and assessment of serum/urine βhCG level
- **Risk categories:** Age, type of antecedent pregnancy, interval months from index pregnancy, pretreatment serum/urine βhCG, diameter of largest tumour, site of metastasis, number of metastases, and previous failed chemotherapy are integrated to provide a prognostic score that divides cases into low and high-risk categories.

**TM Clinical Classification**

**T – Primary Tumour**

<table>
<thead>
<tr>
<th>TM Categories</th>
<th>FIGO Stages</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>TX</td>
<td></td>
<td>Primary tumour cannot be assessed</td>
</tr>
<tr>
<td>T0</td>
<td>I</td>
<td>No evidence of primary tumour</td>
</tr>
<tr>
<td>T1</td>
<td>I</td>
<td>Tumour confined to uterus</td>
</tr>
<tr>
<td>T2(^b)</td>
<td>II</td>
<td>Tumour extends to other genital structures: vagina, ovary, broad ligament, fallopian tube by metastasis or direct extension</td>
</tr>
<tr>
<td>M1a</td>
<td>III</td>
<td>Metastasis to lung(s)</td>
</tr>
<tr>
<td>M1b(^c)</td>
<td>IV</td>
<td>Other distant metastasis</td>
</tr>
</tbody>
</table>

**Notes**

\(^a\) Stages I to IV are subdivided into A and B according to the prognostic score.

\(^b\) Genital metastasis (vagina, ovary, broad ligament, fallopian tube) is classified T2.
Any involvement of non-genital structures, whether by direct invasion or metastasis is described using the M classification.

**pTM Pathological Classification**

The pT categories correspond to the T categories. For pM see page 8.

**Stage**

<table>
<thead>
<tr>
<th>Stage</th>
<th>T</th>
<th>M</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>II</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>III</td>
<td>Any</td>
<td>1a</td>
</tr>
<tr>
<td>IV</td>
<td>Any</td>
<td>1b</td>
</tr>
</tbody>
</table>

**Prognostic Score**

<table>
<thead>
<tr>
<th>Prognostic Factor</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>&lt;40</td>
<td>≥40</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Antecedent pregnancy</td>
<td>H. mole</td>
<td>Abortion</td>
<td>Term pregnancy</td>
<td></td>
</tr>
<tr>
<td>Months from index pregnancy</td>
<td>&lt;4</td>
<td>4–6</td>
<td>7–12</td>
<td>&gt;12</td>
</tr>
<tr>
<td>Pretreatment serum hCG (IU/ml)</td>
<td>&lt;10³</td>
<td>10³–&lt;10⁴</td>
<td>10⁴–&lt;10⁵</td>
<td>&gt;10⁵</td>
</tr>
<tr>
<td>Largest tumour size including uterus</td>
<td>&lt;3.cm</td>
<td>3–5.cm</td>
<td>&gt;5.cm</td>
<td></td>
</tr>
<tr>
<td>Sites of metastasis</td>
<td>Lung</td>
<td>Spleen, kidney</td>
<td>Gastrointestinal tract</td>
<td>Liver, brain</td>
</tr>
<tr>
<td>Number of metastasis</td>
<td>1–4</td>
<td>5–8</td>
<td>&gt;8</td>
<td></td>
</tr>
<tr>
<td>Previous failed chemotherapy</td>
<td></td>
<td>Single drug</td>
<td>Two or more drugs</td>
<td></td>
</tr>
</tbody>
</table>

**Risk categories:**

Total prognostic score 6 or less = low risk
Total score 7 or more = high risk

**Prognostic Group**

Record stage and prognostic score separated by a colon, i.e., II: 4 or IV: 9

**Reference**
Urological Tumours

Introductory Notes

The following sites are included:

- Penis
- Prostate
- Testis
- Kidney
- Renal pelvis and ureter
- Urinary bladder
- Urethra

Each site is described under the following headings:

- Rules for classification with the procedures for assessing T, N, and M categories; additional methods may be used when they enhance the accuracy of appraisal before treatment
- Anatomical sites and subsites where appropriate
- Definition of the regional lymph nodes
- Distant metastasis
- TNM clinical classification
- pTNM pathological classification
- G Histopathological grading where applicable
- Stage
- Prognostic factors grid

Penis

(ICD-O-3 C60)

Rules for Classification

The classification applies only to carcinomas. There should be histological confirmation of the disease.

The following are the procedures for assessing T, N, and M categories:
T categories  Physical examination and endoscopy

N categories  Physical examination and imaging

M categories  Physical examination and imaging

Anatomical Subsites

1. Prepuce (C60.0)
2. Glans penis (C60.1)
3. Body of penis (C60.2)

Regional Lymph Nodes

The regional lymph nodes are the superficial and deep inguinal and the pelvic nodes.

TNM Clinical Classification

T – Primary Tumour

TX  Primary tumour cannot be assessed
To  No evidence of primary tumour
Tis  Carcinoma in situ
Ta  Non invasive verrucous carcinoma*

T1  Tumour invades subepithelial connective tissue
   T1a Tumour invades subepithelial connective tissue without lymphovascular invasion and is not poorly differentiated
   T1b Tumour invades subepithelial connective tissue with lymphovascular invasion or is poorly differentiated
T2  Tumour invades corpus spongiosum with or without invasion of the urethra
T3  Tumour invades corpus cavernosum with or without invasion of the urethra
T4  Tumour invades other adjacent structures

Note

* Verrucous carcinoma not associated with destructive invasion.

N – Regional Lymph Nodes

NX  Regional lymph nodes cannot be assessed
No  No palpable or visibly enlarged inguinal lymph nodes
N1  Palpable mobile unilateral inguinal lymph node
N2  Palpable mobile multiple or bilateral inguinal lymph nodes
N3  Fixed inguinal nodal mass or pelvic lymphadenopathy unilateral or bilateral

M – Distant Metastasis

M0  No distant metastasis
M1  Distant metastasis

pTNM Pathological Classification

The pT categories correspond to the T categories. The pN categories are based upon biopsy, or surgical excision. For pM see page 8.

pNX  Regional lymph nodes cannot be assessed
pN0  No regional lymph node metastasis
pN1  Metastasis in one or two inguinal lymph nodes
pN2  Metastasis in more than two unilateral inguinal nodes or bilateral inguinal lymph nodes
pN3  Metastasis in pelvic lymph node(s), unilateral or bilateral or extranodal extension of regional lymph node metastasis

Stage

<table>
<thead>
<tr>
<th>Stage</th>
<th>Tis</th>
<th>No</th>
<th>Mo</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Ta</td>
<td>No</td>
<td>Mo</td>
</tr>
<tr>
<td>Stage I</td>
<td>T1a</td>
<td>No</td>
<td>Mo</td>
</tr>
<tr>
<td>Stage IIA</td>
<td>T1b,T2</td>
<td>No</td>
<td>Mo</td>
</tr>
<tr>
<td>Stage IIB</td>
<td>T3</td>
<td>No</td>
<td>Mo</td>
</tr>
<tr>
<td>Stage IIIA</td>
<td>T1, T2, T3</td>
<td>N1</td>
<td>Mo</td>
</tr>
<tr>
<td>Stage IIIB</td>
<td>T1, T2, T3</td>
<td>N2</td>
<td>Mo</td>
</tr>
<tr>
<td>Stage IV</td>
<td>T4</td>
<td>Any N Mo</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Any T</td>
<td>N3</td>
<td>Mo</td>
</tr>
<tr>
<td></td>
<td>Any T</td>
<td>Any N M1</td>
<td></td>
</tr>
</tbody>
</table>

Prognostic Factors Grid – Penis
### Prognostic factors for survival for squamous cell carcinoma

<table>
<thead>
<tr>
<th>Prognostic factor</th>
<th>Tumour related</th>
<th>Host related</th>
<th>Environment related</th>
</tr>
</thead>
<tbody>
<tr>
<td>Essential</td>
<td>Differentiation Lymphovascular space invasion Invasion of the corpora</td>
<td>History of genital condylomas Lichen sclerosis PUVA</td>
<td>Poor hygiene</td>
</tr>
<tr>
<td>Additional</td>
<td>HPV/p16 (presence may confer better prognosis)</td>
<td>Smoking HIV/immune suppression</td>
<td></td>
</tr>
<tr>
<td>New and promising</td>
<td>p53 (predicts for lymph node metastases) EGFR</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>


### Prostate

**(ICD-O-3 C61.9)**

#### Rules for Classification

The classification applies only to adenocarcinomas. Transitional cell carcinoma of the prostate is classified as a urethral tumour (see page 208). There should be histological confirmation of the disease.

The following are the procedures for assessing T, N, and M categories:

- **T categories**  Physical examination, imaging, endoscopy, biopsy, and biochemical tests
- **N categories**  Physical examination and imaging
- **M categories**  Physical examination, imaging, skeletal studies, and biochemical tests

#### Regional Lymph Nodes

The regional lymph nodes are the nodes of the true pelvis, which essentially are the pelvic nodes below the bifurcation of the common iliac arteries. Laterality does not affect the N classification.

#### TNM Clinical Classification

**T – Primary Tumour**

- **T0** No evidence of primary tumour
- **T1** Clinically inapparent tumour that is not palpable
**T1**
- T1a: Tumour incidental histological finding in 5% or less of tissue resected
- T1b: Tumour incidental histological finding in more than 5% of tissue resected
- T1c: Tumour identified by needle biopsy (e.g., because of elevated PSA)

**T2**
- T2: Tumour that is palpable and confined within prostate
  - T2a: Tumour involves one half of one lobe or less
  - T2b: Tumour involves more than half of one lobe, but not both lobes
  - T2c: Tumour involves both lobes

**T3**
- T3: Tumour extends through the prostatic capsule*
  - T3a: Extracapsular extension (unilateral or bilateral) including microscopic bladder neck involvement
  - T3b: Tumour invades seminal vesicle(s)

**T4**
- T4: Tumour is fixed or invades adjacent structures other than seminal vesicles: external sphincter, rectum, levator muscles, and/or pelvic wall

**Note**
* Invasion into the prostatic apex or into (but not beyond) the prostatic capsule is not classified as T3, but as T2.

**N** – Regional Lymph Nodes
- NX: Regional lymph nodes cannot be assessed
- N0: No regional lymph node metastasis
- N1: Regional lymph node metastasis

**Note**
Metastasis no larger than 0.2 cm can be designated pNmi. (See Introduction, pN, page 7.)

**M** – Distant Metastasis*
- M0: No distant metastasis
- M1: Distant metastasis
  - M1a: Non-regional lymph node(s)
  - M1b: Bone(s)
  - M1c: Other site(s)

**Note**
* When more than one site of metastasis is present, the most advanced category is used. (p)M1c is the most advanced category.
**pTNM Pathological Classification**

The pT and pN categories correspond to the T and N categories. For pM see page 8. However, there is no pT1 category because there is insufficient tissue to assess the highest pT category or subcategories of pT2.

**G Histopathological Grade Group**\(^1,2\)

GX Grade cannot be assessed

<table>
<thead>
<tr>
<th>Grade Group</th>
<th>Gleason Score</th>
<th>Gleason Pattern</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>(\leq 6)</td>
<td>(\leq 3.+.3)</td>
</tr>
<tr>
<td>2</td>
<td>7</td>
<td>3.+.4</td>
</tr>
<tr>
<td>3</td>
<td>7</td>
<td>4.+.3</td>
</tr>
<tr>
<td>4</td>
<td>8</td>
<td>4.+.4</td>
</tr>
<tr>
<td>5</td>
<td>9–10</td>
<td>4.+.5, 5.+.4, 5.+.5</td>
</tr>
</tbody>
</table>

**Stage*\)

- Stage I: T1, T2a No Mo
- Stage II: T2b, T2c No Mo
- Stage III: T3, T4 No Mo
- Stage IV: Any T N1 Mo
  - Any T Any N M1

**Note**

* The AJCC also publish a prognostic group for prostate tumours.

**Prognostic Factors Grid – Prostate**
## Prognostic factors for prostate cancer

<table>
<thead>
<tr>
<th>Prognostic factor</th>
<th>Tumour related</th>
<th>Host related</th>
<th>Environment related</th>
</tr>
</thead>
<tbody>
<tr>
<td>Essential</td>
<td>Gleason sum score Grade group TNM stage PSA level</td>
<td>Co.morbidity Age Performance status</td>
<td></td>
</tr>
<tr>
<td>Additional</td>
<td>Alkaline phosphatase (if bone metastases) % involvement of cores on biopsy and number of positive cores</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>


## References


## Testis

(ICD-O-3 C62)

### Rules for Classification

The classification applies only to germ cell tumours of the testis. There should be histological confirmation of the disease and division of cases by histological type. Histopathological grading is not applicable.

The presence of elevated serum tumour markers, including alpha fetoprotein (AFP), human chorionic gonadotropin (hCG), and lactate dehydrogenase (LDH), is frequent in this disease. Staging is based on the determination of the anatomic extent of disease and assessment of serum tumour markers.

The following are the procedures for assessing N, M, and S categories:

- **N categories**  Physical examination and imaging
- **M categories**  Physical examination, imaging, and biochemical tests
S categories  Serum tumour markers

Stages are subdivided based on the presence and degree of elevation of serum tumour markers. Serum tumour markers are obtained immediately after orchiectomy and, if elevated, should be performed serially after orchiectomy according to the normal decay for AFP (half-life 7 days) and hCG (half-life 3 days) to assess for serum tumour marker elevation. The S classification is based on the nadir value of hCG and AFP after orchiectomy. The serum level of LDH (but not its half-life levels) has prognostic value in patients with metastatic disease and is included for staging.

Regional Lymph Nodes

The regional lymph nodes are the abdominal paraaortic (periaortic), preaortic, interaortocaval, precaval, paracaval, retrocaval, and retroaortic nodes. Nodes along the spermatic vein should be considered regional. Laterality does not affect the N classification. The intrapelvic nodes and the inguinal nodes are considered regional after scrotal or inguinal surgery.

TNM Clinical Classification

T – Primary tumour

Except for pTis and pT4, where radical orchiectomy is not always necessary for classification purposes, the extent of the primary tumour is classified after radical orchiectomy; see pT. In other circumstances, TX is used if no radical orchiectomy has been performed.

N – Regional Lymph Nodes

NX Regional lymph nodes cannot be assessed
N0 No regional lymph node metastasis
N1 Metastasis with a lymph node mass 2 cm or less in greatest dimension or multiple lymph nodes, none more than 2 cm in greatest dimension
N2 Metastasis with a lymph node mass more than 2 cm but not more than 5 cm in greatest dimension, or multiple lymph nodes, any one mass more than 2 cm but not more than 5 cm in greatest dimension
N3 Metastasis with a lymph node mass more than 5 cm in greatest dimension

M – Distant Metastasis

M0 No distant metastasis
M1 Distant metastasis
M1a Non-regional lymph node(s) or lung metastasis
M1b Distant metastasis other than non-regional lymph nodes and lung
**pTNM Pathological Classification**

**pT – Primary Tumour**

- **pTX** Primary tumour cannot be assessed (see T – Primary Tumour)
- **pTo** No evidence of primary tumour (e.g., histological scar in testis)
- **pTis** Intratubular germ cell neoplasia (carcinoma in situ)

**pT1** Tumour limited to testis and epididymis without vascular/lymphatic invasion; tumour may invade tunica albuginea but not tunica vaginalis

**pT2** Tumour limited to testis and epididymis with vascular/lymphatic invasion, or tumour extending through tunica albuginea with involvement of tunica vaginalis

**pT3** Tumour invades spermatic cord with or without vascular/lymphatic invasion

**pT4** Tumour invades scrotum with or without vascular/lymphatic invasion

**Note**

* AJCC subdivides T1 by T1a and T1b depending on size no greater than 3.0 cm or greater than 3.0 cm in greatest dimension.

**pN – Regional Lymph Nodes**

- **pNX** Regional lymph nodes cannot be assessed
- **pNo** No regional lymph node metastasis
- **pN1** Metastasis with a lymph node mass 2.0 cm or less in greatest dimension and 5 or fewer positive nodes, none more than 2.0 cm in greatest dimension
- **pN2** Metastasis with a lymph node mass more than 2.0 cm but not more than 5.0 cm in greatest dimension; or more than 5 nodes positive, none more than 5.0 cm; or evidence of extranodal extension of tumour
- **pN3** Metastasis with a lymph node mass more than 5.0 cm in greatest dimension

**pM – Distant Metastasis**

For pM see page 8.

**S – Serum Tumour Markers**

- **SX** Serum marker studies not available or not performed
- **So** Serum marker study levels within normal limits

<table>
<thead>
<tr>
<th></th>
<th>LDH</th>
<th>hCG (mIU/ml)</th>
<th>AFP (ng/ml)</th>
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<tr>
<td>S1</td>
<td>&lt;1.5×N</td>
<td>and &lt;5000</td>
<td>and &lt;1000</td>
</tr>
<tr>
<td>S2</td>
<td>1.5–10×N</td>
<td>or 5000–50000</td>
<td>or 1000–10000</td>
</tr>
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</table>
Note
N indicates the upper limit of normal for the LDH assay.

Prognostic group

<table>
<thead>
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<th>pN</th>
<th>pM</th>
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</thead>
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<tr>
<td>0</td>
<td>Tis</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>I</td>
<td>T1–T4</td>
<td>N0</td>
<td>M0</td>
</tr>
<tr>
<td>IA</td>
<td>T1</td>
<td>N0</td>
<td>M0</td>
</tr>
<tr>
<td>IB</td>
<td>T2–T4</td>
<td>N0</td>
<td>M0</td>
</tr>
<tr>
<td>IS</td>
<td>Any T/TX N0</td>
<td>Mo</td>
<td>S1 – S3</td>
</tr>
<tr>
<td>II</td>
<td>Any pT/TX N1 – N3</td>
<td>M0</td>
<td>SX</td>
</tr>
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<td>Mo</td>
<td>S0</td>
</tr>
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<td>S1</td>
</tr>
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<td>Mo</td>
<td>S0</td>
</tr>
<tr>
<td></td>
<td>Any pT/TX N2</td>
<td>Mo</td>
<td>S1</td>
</tr>
<tr>
<td>II</td>
<td>Any pT/TX N3</td>
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<td>S0</td>
</tr>
<tr>
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<td>Any pT/TX N3</td>
<td>Mo</td>
<td>S1</td>
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<tr>
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<td>SX</td>
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<td>M1a</td>
<td>S0</td>
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<td>M1a</td>
<td>S1</td>
</tr>
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<td>Any pT/TX N1–N3</td>
<td>M0</td>
<td>S2</td>
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<td>Any pT/TX Any N</td>
<td>M1a</td>
<td>S2</td>
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<td>IIIC</td>
<td>Any pT/TX N1–N3</td>
<td>M0</td>
<td>S3</td>
</tr>
<tr>
<td></td>
<td>Any pT/TX Any N</td>
<td>M1a</td>
<td>S3</td>
</tr>
<tr>
<td></td>
<td>Any pT/TX Any N</td>
<td>M1b</td>
<td>Any S</td>
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</table>
Prognostic factors for testicular cancer

<table>
<thead>
<tr>
<th>Prognostic factors</th>
<th>Tumour related</th>
<th>Host related</th>
<th>Environment related</th>
</tr>
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<tbody>
<tr>
<td>Essential</td>
<td>Histological type</td>
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</tr>
<tr>
<td></td>
<td>T category</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>N category</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>M category</td>
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</tr>
<tr>
<td></td>
<td>Tumour markers</td>
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<tr>
<td></td>
<td>(AFP, hCG, LDH)</td>
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<tr>
<td></td>
<td>Site of metastases</td>
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<tr>
<td>Additional</td>
<td>Rate of marker decline</td>
<td>Delay in diagnosis</td>
<td>Physician expertise</td>
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<tr>
<td>New and promising</td>
<td>Copy number of i(12p)p53Ki.</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>67Apoptotic index</td>
<td></td>
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</tr>
</tbody>
</table>


Kidney

(ICD-O-3 C64)

Rules for Classification

The classification applies only to renal cell carcinoma. There should be histological confirmation of the disease.

The following are the procedures for assessing T, N, and M categories:

- **T categories**  Physical examination and imaging
- **N categories**  Physical examination and imaging
- **M categories**  Physical examination and imaging

Regional Lymph Nodes

The regional lymph nodes are the hilar, abdominal para.aortic, and paracaval nodes. Laterality does not affect the N categories.

TNM Clinical Classification

T – Primary Tumour

TX Primary tumour cannot be assessed
To No evidence of primary tumour
T1 Tumour 7.cm or less in greatest dimension, limited to the kidney
   T1a Tumour 4.cm or less
   T1b Tumour more than 4.cm but not more than 7.cm
T2 Tumour more than 7.cm in greatest dimension, limited to the kidney
   T2a Tumour more than 7.cm but not more than 10.cm
   T2b Tumour more than 10.cm, limited to the kidney
T3 Tumour extends into major veins or perinephric tissues but not into the ipsilateral adrenal gland and not beyond Gerota fascia
   T3a Tumour grossly extends into the renal vein or its segmental (muscle containing) branches, or tumour invades perirenal and/or renal sinus fat (peripelvic) fat but not beyond Gerota fascia
   T3b Tumour grossly extends into vena cava below diaphragm
   T3c Tumour grossly extends into vena cava above the diaphragm or invades the wall of the vena cava
T4 Tumour invades beyond Gerota fascia (including contiguous extension into the ipsilateral adrenal gland)

N – Regional Lymph Nodes
   NX Regional lymph nodes cannot be assessed
   N0 No regional lymph node metastasis
   N1 Metastasis in regional lymph node(s)

M – Distant Metastasis
   Mo No distant metastasis
   M1 Distant metastasis

pTNM Pathological Classification
The pT and pN categories correspond to the T and N categories. For pM see page 8.

Stage

<table>
<thead>
<tr>
<th>Stage</th>
<th>pT</th>
<th>pN</th>
<th>pM</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage I</td>
<td>T1</td>
<td>No</td>
<td>Mo</td>
</tr>
<tr>
<td>Stage II</td>
<td>T2</td>
<td>No</td>
<td>Mo</td>
</tr>
<tr>
<td>Stage III</td>
<td>T3</td>
<td>No</td>
<td>Mo</td>
</tr>
<tr>
<td></td>
<td>T1, T2, T3</td>
<td>N1</td>
<td>Mo</td>
</tr>
<tr>
<td>Stage IV</td>
<td>T4</td>
<td>Any N</td>
<td>Mo</td>
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</tbody>
</table>
## Prognostic Factors Grid – Kidney

Prognostic factors for cancers of the kidney

<table>
<thead>
<tr>
<th>Prognostic factors</th>
<th>Tumour related</th>
<th>Host related</th>
<th>Environment related</th>
</tr>
</thead>
<tbody>
<tr>
<td>Essential</td>
<td>Stage</td>
<td>Surgical candidacy</td>
<td></td>
</tr>
<tr>
<td>Additional</td>
<td>Histological subtype Fuhrman grade (clear cell RCC only)</td>
<td>Performance status Hereditary diseases</td>
<td>Lymph node dissection Adrenalectomy Metastatectomy Immunotherapy/targeted therapy</td>
</tr>
<tr>
<td>Investigational</td>
<td>DNA ploidy Genetic alterations Molecular markers</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>


## Renal Pelvis and Ureter

(ICD-O-3 C65, C66)

### Rules for Classification

The classification applies to carcinomas. Papilloma is excluded. There should be histological or cytological confirmation of the disease.

The following are the procedures for assessing T, N, and M categories:

- **T categories**  Physical examination, imaging, and endoscopy
- **N categories**  Physical examination and imaging
- **M categories**  Physical examination and imaging

### Anatomical Sites

1. Renal pelvis (C65)
2. Ureter (C66)

### Regional Lymph Nodes
The regional lymph nodes are the hilar, abdominal paraaortic, and paracaval nodes and, for ureter, intrapelvic nodes. Laterality does not affect the N classification.

**TNM Clinical Classification**

**T – Primary Tumour**

- **TX** Primary tumour cannot be assessed
- **T0** No evidence of primary tumour
- **Ta** Non-invasive papillary carcinoma
- **Tis** Carcinoma in situ

- **T1** Tumour invades subepithelial connective tissue
- **T2** Tumour invades muscularis
- **T3 (Renal pelvis)** Tumour invades beyond muscularis into peripelvic fat or renal parenchyma
  - *(Ureter)* Tumour invades beyond muscularis into periureteric fat
- **T4** Tumour invades adjacent organs or through the kidney into perinephric fat

**N – Regional Lymph Nodes**

- **NX** Regional lymph nodes cannot be assessed
- **N0** No regional lymph node metastasis
- **N1** Metastasis in a single lymph node 2 cm or less in greatest dimension
- **N2** Metastasis in a single lymph node more than 2 cm, or multiple lymph nodes

**M – Distant Metastasis**

- **M0** No distant metastasis
- **M1** Distant metastasis

**pTNM Pathological Classification**

The pT and pN categories correspond to the T and N categories. For pM see page 8.

**Stage**

- **Stage 0a** Ta No Mo
- **Stage 0is** Tis No Mo
- **Stage I** T1 No Mo
- **Stage II** T2 No Mo
Stage III  T3    No    Mo
Stage IV  T4    No    Mo
Any T    N1, N2 Mo
Any T    Any N   M1

**Urinary Bladder**

**Rules for Classification**

The classification applies to carcinomas. Papilloma is excluded. There should be histological or cytological confirmation of the disease.

The following are the procedures for assessing T, N, and M categories:

- **T categories**  Physical examination, imaging, and endoscopy
- **N categories**  Physical examination and imaging
- **M categories**  Physical examination and imaging

**Regional Lymph Nodes**

The regional lymph nodes are the nodes of the true pelvis, which essentially are the pelvic nodes below the bifurcation of the common iliac arteries. Laterality does not affect the N classification.

**TNM Clinical Classification**

**T – Primary Tumour**

The suffix (m) should be added to the appropriate T category to indicate multiple tumours. The suffix (is) may be added to any T to indicate presence of associated carcinoma in situ.

- **TX**         Primary tumour cannot be assessed
- **T0**        No evidence of primary tumour
- **Ta**        Non-invasive papillary carcinoma
- **Tis**       Carcinoma in situ: ‘flat tumour’

**T1** Tumour invades subepithelial connective tissue
**T2** Tumour invades muscle
  - **T2a** Tumour invades superficial muscle (inner half)
  - **T2b** Tumour invades deep muscle (outer half)
**T3** Tumour invades perivesical tissue:
T3a  microscopically
T3b  macroscopically (extravesical mass)

T4  Tumour invades any of the following: prostate stroma, seminal vesicles, uterus, vagina, pelvic wall, abdominal wall
  T4a  Tumour invades prostate stroma, seminal vesicles, uterus or vagina
  T4b  Tumour invades pelvic wall or abdominal wall

**N – Regional Lymph Nodes**

NX  Regional lymph nodes cannot be assessed
N0  No regional lymph node metastasis
N1  Metastasis in a single lymph node in the true pelvis (hypogastric, obturator, external iliac, or presacral)
N2  Metastasis in multiple regional lymph nodes in the true pelvis (hypogastric, obturator, external iliac, or presacral)
N3  Metastasis in a common iliac lymph node(s)

**M – Distant Metastasis**

M0  No distant metastasis
   M1a  Non-regional lymph nodes
   M1b  Other distant metastasis

**pTNM Pathological Classification**

The pT and pN categories correspond to the T and N categories. For pM see page 8.

**Stage**

<table>
<thead>
<tr>
<th>Stage</th>
<th>pT</th>
<th>pN</th>
<th>pM</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage 0a</td>
<td>Ta</td>
<td>No</td>
<td>Mo</td>
</tr>
<tr>
<td>Stage 0is</td>
<td>Tis</td>
<td>No</td>
<td>Mo</td>
</tr>
<tr>
<td>Stage I</td>
<td>T1</td>
<td>No</td>
<td>Mo</td>
</tr>
<tr>
<td>Stage II</td>
<td>T2a, T2b</td>
<td>No</td>
<td>Mo</td>
</tr>
<tr>
<td>Stage IIIA</td>
<td>T3a, T3b, T4a</td>
<td>No</td>
<td>Mo</td>
</tr>
<tr>
<td></td>
<td>T1,T2, T3, T4a</td>
<td>N1</td>
<td>Mo</td>
</tr>
<tr>
<td>Stage IIIB</td>
<td>T1, T2, T3, T4a</td>
<td>N2, N3</td>
<td>Mo</td>
</tr>
<tr>
<td>Stage IVA</td>
<td>T4b</td>
<td>No</td>
<td>Mo</td>
</tr>
<tr>
<td></td>
<td>Any T</td>
<td>Any N</td>
<td>M1a</td>
</tr>
<tr>
<td>Stage IVB</td>
<td>Any T</td>
<td>Any N</td>
<td>M1b</td>
</tr>
</tbody>
</table>
## Prognostic Factors Grid – Bladder

Prognostic factors for progression to invasive disease in superficial bladder cancer (Ta, T1, Tis)

<table>
<thead>
<tr>
<th>Prognostic factor</th>
<th>Tumour related</th>
<th>Host related</th>
<th>Environment related</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Essential</strong></td>
<td>Grade T stage Carcinoma <em>in situ</em> (Cis) Number of lesions Previous recurrences</td>
<td>Age Performance status Other co. morbidities</td>
<td>Extent of transurethral resection (Intravesical chemotherapy reduces recurrence but limited evidence for reducing progression)</td>
</tr>
<tr>
<td><strong>Additional</strong></td>
<td>Tumour size Recurrence at 3. month check</td>
<td>Gender Continued tobacco use</td>
<td></td>
</tr>
<tr>
<td><strong>Novel/promising</strong></td>
<td>p53NMP22FGFR3 mutation status COX.2 (especially upper tract) Claudin protein family members DNA methylation status Lymphovascular invasion Extent of invasion (T1microinvasive or T1extensive invasive)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Note: The table provides a comprehensive overview of factors influencing the progression of superficial bladder cancer. Essential factors include grade, T stage, and disease stage, while additional factors such as tumour size and recurrence status are also considered. Novel/promising factors include genetic and molecular markers such as p53 and FGFR3 mutation status.*
### Prognostic factors for metastatic risk and survival in invasive, locally advanced and/or node positive bladder cancer (T2–4, N0–1)

<table>
<thead>
<tr>
<th>Prognostic factors</th>
<th>Tumor related</th>
<th>Host related</th>
<th>Environment related</th>
</tr>
</thead>
<tbody>
<tr>
<td>Essential</td>
<td>T category</td>
<td>Age Performance status</td>
<td>Surgical margin status</td>
</tr>
<tr>
<td></td>
<td>N category</td>
<td>ALP Other co. morbidities</td>
<td></td>
</tr>
<tr>
<td>Additional</td>
<td>Grade</td>
<td>Haemoglobin Response of primary to chemotherapy</td>
<td>Extent of lymph node resection</td>
</tr>
<tr>
<td></td>
<td>Histological type</td>
<td></td>
<td>Proportion (density) of involved lymph nodes</td>
</tr>
<tr>
<td></td>
<td>Lymphovascular invasion</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Concomitant Cis</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Tumour size</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Hydronephrosis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Novel/promising</td>
<td>p53, p63, p21 (for long term bladder preservation) Rb protein</td>
<td>Certain germline singlenucleotide polymorphisms (SNPs)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Ki67 EGF receptor</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>HER2 expression E cadherin</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Microvessel density</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Treatment resistance mechanisms (ERCC1, BRCA1 or MMR mutations)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

With established metastatic disease, visceral metastasis is associated with a poorer prognosis.


## Urethra

*(ICD-O-3 C68.0, C61.9)*

### Rules for Classification

The classification applies to carcinomas of the urethra (ICD.O C68.0) and transitional cell carcinomas of the prostate (ICD.O C61.9) and prostatic urethra. There should be histological or cytological confirmation of the disease.

The following are the procedures for assessing T, N, and M categories:

- **T categories**  Physical examination, imaging, and endoscopy
- **N categories**  Physical examination and imaging
Regional Lymph Nodes
The regional lymph nodes are the inguinal and the pelvic nodes. Laterality does not affect the N classification.

TNM Clinical Classification

T – Primary Tumour

TX Primary tumour cannot be assessed
To No evidence of primary tumour

Urethra (male and female)
Ta Non-invasive papillary, polypoid, or verrucous carcinoma
Tis Carcinoma in situ

T1 Tumour invades subepithelial connective tissue
T2 Tumour invades any of the following: corpus spongiosum, prostate, periurethral muscle
T3 Tumour invades any of the following: corpus cavernosum, beyond prostatic capsule, anterior vagina, bladder neck (extraprostatic extension)
T4 Tumour invades other adjacent organs (invasion of the bladder)

Urothelial (transitional cell) carcinoma of the prostate
Tis pu Carcinoma in situ, involvement of prostatic urethra
Tis pd Carcinoma in situ, involvement of prostatic ducts

T1 Tumour invades subepithelial connective tissue (for tumours involving prostatic urethra only)
T2 Tumour invades any of the following: prostatic stroma, corpus spongiosum, periurethral muscle
T3 Tumour invades any of the following: corpus cavernosum, beyond prostatic capsule, bladder neck (extraprostatic extension)
T4 Tumour invades other adjacent organs (invasion of the bladder or rectum)

N – Regional Lymph Nodes

NX Regional lymph nodes cannot be assessed
No No regional lymph node metastasis
N1 Metastasis in a single lymph node
N2 Metastasis in multiple lymph nodes

M – Distant Metastasis

M0 No distant metastasis
M1 Distant metastasis

pTNM Pathological Classification

The pT and pN categories correspond to the T and N categories. For pM see page 8.

Stage

Stage 0a Ta No Mo
Stage 0is Tis No Mo
Stage I T1 No Mo
Stage II T2 No Mo
Stage III T1, T2 N1 Mo
   T3 No, N1 Mo
Stage IV T4 No, N1 Mo
   Any T N2 Mo
   Any T Any N M1
Adrenal Cortex (ICD-O-3 C74.0)

Rules for Classification
This classification applies only to carcinomas of the adrenal cortex. It does not apply to tumours of the adrenal medulla or sarcomas.
The following are the procedures for assessing T, N, and M categories:

- **T categories**  Physical examination and imaging
- **N categories**  Physical examination and imaging
- **M categories**  Physical examination and imaging

Regional Lymph Nodes
The regional lymph nodes are the hilar, abdominal paraaortic, and paracaval nodes. Laterality does not affect the N categories.

TNM Clinical Classification

T – Primary Tumour

- **TX** Primary tumour cannot be assessed
- **T0** No evidence of primary tumour
- **T1** Tumour 5.0 cm or less in greatest dimension, no extra adrenal invasion
- **T2** Tumour greater than 5.0 cm, no extra adrenal invasion
- **T3** Tumour of any size with local invasion, but not invading adjacent organs*
- **T4** Tumour of any size with invasion of adjacent organs*

Note
* Adjacent organs include kidney, diaphragm, great vessels (renal vein or vena cava), pancreas, and liver.

N – Regional lymph nodes

- **NX** Regional lymph nodes cannot be assessed
- **N0** No regional lymph node metastasis
- **N1** Metastasis in regional lymph node(s)

M – Distant Metastasis

- **M0** No distance metastasis
M1. Distant metastasis

**pTNM Pathological Classification**

The pT and pN categories correspond to the T and N categories. For pM see page 8.

**Stage**

<table>
<thead>
<tr>
<th>Stage</th>
<th>T</th>
<th>N</th>
<th>M</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>T1</td>
<td>No</td>
<td>M0</td>
</tr>
<tr>
<td>II</td>
<td>T2</td>
<td>No</td>
<td>M0</td>
</tr>
<tr>
<td>III</td>
<td>T1, T2</td>
<td>N1</td>
<td>M0</td>
</tr>
<tr>
<td></td>
<td>T3, T4</td>
<td>No, N1</td>
<td>M0</td>
</tr>
<tr>
<td>IV</td>
<td>Any T</td>
<td>Any N</td>
<td>M1</td>
</tr>
</tbody>
</table>

**Prognostic Factors Grid**

Prognostic factors for survival in ACC

<table>
<thead>
<tr>
<th>Prognostic factors</th>
<th>Tumour related factors</th>
<th>Host related</th>
<th>Environment related</th>
</tr>
</thead>
<tbody>
<tr>
<td>Essential</td>
<td>T, N, M categories Biochemical status:</td>
<td>Resectability</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Improved survival in patients with functional tumours</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Additional</td>
<td>Response to mitotane</td>
<td>Age</td>
<td></td>
</tr>
<tr>
<td>New and promising</td>
<td>Molecular profile:</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Higher tumour grade, described by Ki.67 or mitotic rate is associated with poorer prognosis</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Chromosomal aberrations associated with poor survival: gain in chromosomes 6, 7, 12 and 19; and loss in chromosomes 3, 8, 10, 16, 17 and 19</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Increasing degree of aberration is associated with shorter survival</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Ophthalmic Tumours

Introductory Notes

Tumours of the eye and its adnexa are a disparate group including carcinoma, melanoma, sarcomas, and retinoblastoma. For clinical convenience they are classified in one section. The following sites are included:

- Eyelid (eyelid tumours are classified with skin tumours)
- Conjunctiva
- Uvea
- Retina
- Orbit
- Lacrimal gland

For histological nomenclature and diagnostic criteria, reference to the WHO histological classification is recommended.¹

Each tumour type is described under the following headings:

- Rules for classification with the procedures for assessing the T, N, and M categories
- Anatomical sites where appropriate
- Definition of the regional lymph nodes
- TNM clinical classification
- pTNM pathological classification
- Stage where applicable
- Prognostic factors grid

Reference


Carcinoma of Conjunctiva

(ICD-O-3 C 69.0)

Rules for Classification
There should be histological confirmation of the disease and division of cases by histological type, for example, mucoepidermoid and squamous cell carcinoma. The following are the procedures for assessing T, N, and M categories:

\[
T \text{ categories } \quad \text{Physical examination}
\]

\[
N \text{ categories } \quad \text{Physical examination}
\]

\[
M \text{ categories } \quad \text{Physical examination and imaging}
\]

**Regional Lymph Nodes**
The regional lymph nodes are the preauricular, submandibular and cervical lymph nodes.

**TNM Clinical Classification**

**T – Primary Tumour**

\[
TX \quad \text{Primary tumour cannot be assessed}
\]

\[
T0 \quad \text{No evidence of primary tumour}
\]

\[
Tis \quad \text{Carcinoma in situ}
\]

\[
T1 \quad \text{Tumour 5.0 mm or less in greatest dimension invades through the conjunctival basement membrane}
\]

\[
T2 \quad \text{Tumour more than 5.0 mm in greatest dimension, invades through the conjunctival basement membrane without invasion of adjacent structures*}
\]

\[
T3 \quad \text{Tumour invades adjacent structures*}
\]

\[
T4 \quad \text{Tumour invades the orbit or beyond}
\]

\[
T4a \quad \text{Tumour invades orbital soft tissues, without bone invasion}
\]

\[
T4b \quad \text{Tumour invades bone}
\]

\[
T4c \quad \text{Tumour invades adjacent paranasal sinuses}
\]

\[
T4d \quad \text{Tumour invades brain}
\]

**Note**

* Adjacent structures include: the cornea (3, 6, 9, or 12 clock hours), intraocular compartments, forniceal conjunctiva (lower and/or upper), palpebral conjunctiva (lower and/or upper), tarsal conjunctiva (lower and/or upper), lacrimal punctum and canaliculi (lower and/or upper), plica, caruncle, posterior eyelid lamella, anterior eyelid lamella and/or eyelid margin (lower and/or upper).

**N – Regional Lymph Nodes**

\[
NX \quad \text{Regional lymph nodes cannot be assessed}
\]
M – Distant Metastasis

$M_0$ No distant metastasis
$M_1$ Distant metastasis

**pTNM Pathological Classification**
The $pT$ and $pN$ categories correspond to the $T$ and $N$ categories. For $pM$ see page 8.

**Stage**
No stage is at present recommended.

**Malignant Melanoma of Conjunctiva**
(ICD-O-3 C69.0)

**Rules for Classification**
The classification applies only to conjunctival malignant melanoma. There should be histological confirmation of the disease.
The following are the procedures for assessing $T$, $N$, and $M$ categories:

$T$ categories  Physical examination
$N$ categories  Physical examination
$M$ categories  Physical examination and imaging

**Regional Lymph Nodes**
The regional lymph nodes are the preauricular, submandibular, and cervical lymph nodes.

**TNM Clinical Classification**

**T – Primary Tumour**

$TX$ Primary tumour cannot be assessed
$T_0$ No evidence of primary tumour
$T_{is}$ Melanoma confined to the conjunctival epithelium (in situ)$^a$

$T_1$ Melanoma of the bulbar conjunctiva

$T_{1a}$ Tumour involves less than or equal to one quadrant$^b$
T1b Tumour involves more than one but less than or equal to two quadrants
T1c Tumour involves more than two but less than or equal to three quadrants
T1d Tumour involves more than three quadrants

T2 Malignant conjunctival melanoma of the non-bulbar conjunctiva involving palpebral, forniceal, and/or caruncular conjunctiva
T2a Non-caruncular tumour involves less than or equal to one quadrant
T2b Non-caruncular tumour involves more than one quadrant
T2c Caruncular tumour involves less than or equal to one quadrant of conjunctiva
T2d Caruncular tumour involves more than one quadrant of conjunctiva

T3 Tumour with local invasion into:
T3a Globe
T3b Eyelid
T3c Orbit
T3d Paranasal sinus, nasolacrimal duct, and/or lacrimal gland

T4 Tumour invades central nervous system

Notes

a Melanoma in situ (includes the term primary acquired melanosis) with atypia replacing greater than 75% of the normal epithelial thickness with cytological features of epithelial cells, including abundant cytoplasm, vesicular nuclei, or prominent nucleoli, and/or presence of intraepithelial nest of atypical cells.

b Quadrants are defined by clock hour, starting at the limbus (e.g., 6, 9, 12, 3) extending from the central cornea, to and beyond the eyelid margins. This will bisect the caruncle.

N – Regional Lymph Nodes
   NX Regional lymph nodes cannot be assessed
   N0 No regional lymph node metastasis
   N1 Regional lymph node metastasis

M – Distant Metastasis
   M0 No distant metastasis
   M1 Distant metastasis

pTNM Pathological Classification
**pT – Primary Tumour**

- **pTX** Primary tumour cannot be assessed
- **pT0** No evidence of primary tumour
- **pTis** Melanoma confined to the conjunctival epithelium (in situ) *

**pT1** Melanoma of the bulbar conjunctiva
- **pT1a** Tumour 2.0 mm or less in thickness with invasion of the substantia propria
- **pT1b** Tumour more than 2.0 mm in thickness with invasion of the substantia propria

**pT2** Melanoma of the palpebral, forniceal or caruncular conjunctiva
- **pT2a** Tumour 2.0 mm or less in thickness with invasion of the substantia propria
- **pT2b** Tumour more than 2.0 mm in thickness with invasion of the substantia propria

**pT3** Melanoma invades the eye, eyelid, nasolacrimal system or orbit
- **pT3a** Invades the globe
- **pT3b** Invade the eyelid
- **pT3c** Invades the orbit
- **pT3d** Invades the paranasal sinus and/or nasolacrimal duct or lacrimal sac

**pT4** Melanoma invades central nervous system

**Note**

* pTis Melanoma in situ (includes the term primary acquired melanosis) with atypia replacing greater than 75% of the normal epithelial thickness, with cytological features of epithelioid cells, including abundant cytoplasm, vesicular nuclei or prominent nucleoli, and/or presence of intraepithelial nests of atypical cells.

**pN – Regional Lymph Nodes**
The pN categories correspond to the N categories.

**pM – Distant Metastasis**
For pM categories see page 8.

**G – Histopathological Grading**
Histological grade represents the origin of the primary tumour.

- **GX** Origin cannot be assessed
- **G0** Primary acquired melanosis without cellular atypia
- **G1** Conjunctival nevus
G2  Primary acquired melanosis with cellular atypia (epithelial disease only)
G3  Primary acquired melanosis with epithelial cellular atypia and invasive melanoma
G4  De novo malignant melanoma

Stage
No stage is at present recommended.

Malignant Melanoma of Uvea
(ICD-O C69.3,4)

Rules for Classification
There should be histological confirmation of the disease.
The following are the procedures for assessing T, N, and M categories:

\[ T \]  Physical examination; additional methods such as fluorescein angiography
\[ N \]  Physical examination
\[ M \]  Examination and imaging

Regional Lymph Nodes
The regional lymph nodes are the preauricular, submandibular, and cervical nodes.

Anatomical Sites
1. Iris (C69.4)
2. Ciliary body (C69.4)
3. Choroid (C69.3)

TNM Clinical Classification

T – Primary Tumour

\[ TX \] Primary tumour cannot be assessed
\[ T0 \] No evidence of primary tumour

Iris*
T1  Tumour limited to iris
   T1a  not more than 3 clock hours in size
   T1b  more than 3 clock hours in size
   T1c  with secondary glaucoma
T2  Tumour confluent with or extending into the ciliary body, choroid, or both
   T2a  Tumour confluent with or extending into the ciliary body without secondary glaucoma
   T2b  Tumour confluent with or extending into the choroid without secondary glaucoma
   T2c  Tumour confluent with or extending into the ciliary body and/or choroid with secondary glaucoma
T3  Tumour confluent with or extending into the ciliary body, choroid or both, with scleral extension
T4  Tumour with extrascleral extension
   T4a  less than or equal to 5.0 mm in diameter
   T4b  more than 5.0 mm in diameter

Note
* Iris melanomas originate from, and are predominantly located in, this region of the uvea. If less than half of the tumour volume is located within the iris, the tumour may have originated in the ciliary body and consideration should be given to classifying it accordingly.

Ciliary Body and Choroid
Primary ciliary body and choroidal melanomas are classified according to the four tumour size categories listed in this section.
**Figure 1** Classification for ciliary body and choroid uveal melanoma based on thickness and diameter.

<table>
<thead>
<tr>
<th>T1</th>
<th>Tumour size category 1</th>
</tr>
</thead>
<tbody>
<tr>
<td>T1a</td>
<td>without ciliary body involvement and extraocular extension</td>
</tr>
<tr>
<td>T1b</td>
<td>with ciliary body involvement</td>
</tr>
<tr>
<td>T1c</td>
<td>without ciliary body involvement but with extraocular extension less than or equal to 5 mm in diameter</td>
</tr>
<tr>
<td>T1d</td>
<td>with ciliary body involvement and extraocular extension less than or equal to 5 mm in diameter</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>T2</th>
<th>Tumour size category 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>T2a</td>
<td>without ciliary body involvement and extraocular extension</td>
</tr>
<tr>
<td>T2b</td>
<td>with ciliary body involvement</td>
</tr>
<tr>
<td>T2c</td>
<td>without ciliary body involvement but with extraocular extension less than or equal to 5 mm in diameter</td>
</tr>
<tr>
<td>T2d</td>
<td>with ciliary body involvement and extraocular extension less than or equal to 5 mm in diameter</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>T3</th>
<th>Tumour size category 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>T3a</td>
<td>without ciliary body involvement and extraocular extension</td>
</tr>
<tr>
<td>T3b</td>
<td>with ciliary body involvement</td>
</tr>
<tr>
<td>T3c</td>
<td>without ciliary body involvement but with extraocular extension less than or equal to 5 mm in diameter</td>
</tr>
<tr>
<td>T3d</td>
<td>with ciliary body involvement and extraocular extension less than or equal to 5 mm in diameter</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>T4</th>
<th>Tumour size category 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>T4a</td>
<td>without ciliary body involvement and extraocular extension</td>
</tr>
<tr>
<td>T4b</td>
<td>with ciliary body involvement</td>
</tr>
<tr>
<td>T4c</td>
<td>without ciliary body involvement but with extraocular extension less than or equal to 5 mm in diameter</td>
</tr>
</tbody>
</table>

Largest basal diameter (mm)

<table>
<thead>
<tr>
<th>Thickness (mm)</th>
<th>12.1–15.0</th>
<th>9.1–12.0</th>
<th>6.1–9.0</th>
<th>3.1–6.0</th>
<th>≤ 3.0</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;15</td>
<td>4</td>
<td>4</td>
<td>4</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>12.1–15.0</td>
<td>3</td>
<td>3</td>
<td>4</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>9.1–12.0</td>
<td>2</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>6.1–9.0</td>
<td>2</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>3.1–6.0</td>
<td>1</td>
<td>2</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>≤ 3.0</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>2</td>
<td>2</td>
</tr>
</tbody>
</table>

[^1]: Largest basal diameter (mm)
equal to 5.0 mm in diameter
T4d with ciliary body involvement and extraocular extension less than or equal to 5.0 mm in diameter
T4e Any tumour size category with extraocular extension more than 5.0 mm in diameter

Notes

a In clinical practice, the largest tumour basal diameter may be estimated in optic disc diameters (dd, average: 1 dd = 1.5 mm). Tumour thickness may be estimated in diopters (average: 2.5 diopters = 1 mm). However, techniques such as ultrasonography and fundus photography are used to provide more accurate measurements. Ciliary body involvement can be evaluated by the slit lamp, ophthalmoscopy, gonioscopy, and transillumination. However, high-frequency ultrasonography (ultrasound biomicroscopy) is used for more accurate assessment. Extension through the sclera is evaluated visually before and during surgery, and with ultrasonography, computed tomography, or magnetic resonance imaging.

b When histopathological measurements are recorded after fixation, tumour diameter and thickness may be underestimated because of tissue shrinkage.

N – Regional Lymph Nodes

NX Regional lymph nodes cannot be assessed
N0 No regional lymph node metastasis
N1 Regional lymph node metastasis

M – Distant Metastasis

M0 No distant metastasis
M1 Distant metastasis
  M1a Largest metastases 3.0 cm or less in greatest dimension
  M1b Largest metastases is larger than 3.0 cm in greatest dimension but not larger than 8.0 cm
  M1c Largest metastases is larger than 8.0 cm in greatest dimension

pTNM Pathological Classification

The pT and pN categories correspond to the T and N categories. For pM see page 8.

Stage

Stage I   T1a   No   Mo
Stage IIA  T1b–d, T2a  No  Mo
Stage IIB  T2b, T3a  No  Mo
Stage IIIA T2c–d
    T3b–c  No  Mo
    T4a  No  Mo
Stage IIIB T3d
    T4b–c  No  Mo
Stage IIIC T4d–e  No  Mo
Stage IV  Any T  N1  Mo
    Any T  Any N  M1

Prognostic Factors Grid

Prognostic factors for survival for uveal melanoma

<table>
<thead>
<tr>
<th>Prognostic factors</th>
<th>Tumour related</th>
<th>Host related</th>
<th>Environment related</th>
</tr>
</thead>
<tbody>
<tr>
<td>Essential</td>
<td>Largest tumour diameter (typically width)</td>
<td></td>
<td>Advanced age</td>
</tr>
<tr>
<td></td>
<td>Higher UICC T category (associated with worse survival)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Additional</td>
<td>Extrascleral ‘extraocular’ extension</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Location (iris tumours are typically smaller at diagnosis, while ciliary body tumours are less visible and typically larger at diagnosis)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Histopathological cell type (spindle cell more favourable than epithelioid)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Mitotic activity</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Microvasculature patterns</td>
<td></td>
<td></td>
</tr>
<tr>
<td>New and promising</td>
<td>PET.CT standardized uptake value (SUV): higher SUV associated with worse prognosis</td>
<td></td>
<td>Immunotherapy</td>
</tr>
<tr>
<td></td>
<td>Monosomy 3, abnormalities of chromosomes 6 and 8*</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Genetic expression profiling (class 1 more favourable than 1A and 2)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Test has been independently confirmed at multiple centres.

Retinoblastoma

Rules for Classification

In bilateral cases, the eyes should be classified separately. The classification does not apply to complete spontaneous regression of the tumour. There should be histological confirmation of the disease in an enucleated eye.

The following are the procedures for assessing T, N, and M categories:

- **T** categories
  - Physical examination and imaging

- **N** categories
  - Physical examination

- **M** categories
  - Physical examination and imaging; examination of bone marrow and cerebrospinal fluid may enhance the accuracy of appraisal

Regional Lymph Nodes

The regional lymph nodes are the preauricular, submandibular, and cervical lymph nodes.

TNM Clinical Classification

**T – Primary Tumour**

- **TX** Primary tumour cannot be assessed.
- **T0** No evidence of primary tumour.

- **T1** Tumour confined to the retina with subretinal fluid no more than 5 mm from the base of any tumour, without retinal detachment
  - **T1a** No tumour in either eye is greater than 3 mm in largest dimension or located closer than 1.5 mm to the optic nerve or fovea
  - **T1b** At least one tumour is greater than 3 mm in largest dimension or located closer than 1.5 mm to the optic nerve or fovea. No retinal detachment or subretinal fluid beyond 5 mm from the base of the tumour

- **T2** Tumours with vitreous or subretinal seeding or retinal detachment
  - **T2a** Tumour with subretinal fluid more than 5 mm from the base of any tumour
  - **T2b** Tumour with vitreous and/or subretinal seeding

- **T3** Severe intraocular disease
  - **T3a** Phthisis or prephthisis bulbi
  - **T3b** Invasion of: choroid, pars plana, ciliary body, lens, zonules, iris or anterior chamber
T3c Raied intraocular pressure with neovascularization and/or buphthalmos
T3d Hyphema and or massive vitreous haemorrhage
T3e Aseptic orbital cellulitis
T4 Extraocular tumour
   T4a Invasion of optic nerve or orbital tissues
   T4b Extraocular invasion with proptosis and/or orbital mass

N – Regional Lymph Nodes
   NX Regional lymph nodes cannot be assessed
   N0 No regional lymph node metastasis
   N1 Regional lymph node metastasis

M – Distant Metastasis
   M0 No distant metastasis
   M1 Distant metastasis
      M1a Single or multiple metastasis to sites other than CNS or brain
      M1b Metastasis to the CNS including brain

TNM Pathological Classification

T – Primary Tumour
   pTX Primary tumour cannot be assessed
   pT0 No evidence of primary tumour
   pT1 Tumour confined to eye with no optic nerve or choroidal invasion
   pT2 Tumour with intraocular invasion
      pT2a Focal choroidal invasion and pre. or intralaminar invasion of the optic nerve head
      pT2b Tumour invasion of stroma of iris and/or trabecular meshwork and/or Schlemm’s canal
   pT3 Tumour with significant local invasion
      pT3a Choroidal invasion larger than 3. mm in diameter or multiple foci of invasion totalling more than 3. mm or any full.thickness involvement
      pT3b Retrolaminar invasion of optic nerve without invasion of transected end of optic nerve
      pT3c Partial.thickness involvement of sclera within the inner two.thirds
      pT3d Full.thickness invasion into outer third of the sclera and/or invasion into or
around emissary channels

pT4 Extraocular extension: Tumour invades optic nerve at transected end, in meningeal space around the optic nerve, full thickness invasion of the sclera with invasion of the episclera, adipose tissue, extraocular muscle, bone, conjunctiva, or eyelid.

**N – Regional Lymph Nodes**

- pNX Regional lymph nodes cannot be assessed
- pNo No regional lymph node involvement
- pN1 Regional lymph node involvement

**pM – Metastasis**

- cMo No distant metastasis
- pM1 Distant metastasis
  - pM1a Single or multiple metastasis to sites other than CNS
  - pM1b Metastasis to CNS parenchyma or CSF fluid

**Stage**

**Clinical Stage**

<table>
<thead>
<tr>
<th>Stage</th>
<th>T1, T2, T3</th>
<th>N0</th>
<th>M0</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage I</td>
<td>T1, T2, T3</td>
<td>N0</td>
<td>M0</td>
</tr>
<tr>
<td>Stage II</td>
<td>T4a</td>
<td>N0</td>
<td>M0</td>
</tr>
<tr>
<td>Stage III</td>
<td>T4b</td>
<td>N0</td>
<td>M0</td>
</tr>
<tr>
<td></td>
<td>Any T</td>
<td>N1</td>
<td>M0</td>
</tr>
<tr>
<td>Stage IV</td>
<td>Any T</td>
<td>Any N</td>
<td>M1</td>
</tr>
</tbody>
</table>

**Pathological Stage**

<table>
<thead>
<tr>
<th>Stage</th>
<th>T1, T2, T3</th>
<th>N0</th>
<th>M0</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage I</td>
<td>T1, T2, T3</td>
<td>N0</td>
<td>M0</td>
</tr>
<tr>
<td>Stage II</td>
<td>T4</td>
<td>N0</td>
<td>M0</td>
</tr>
<tr>
<td>Stage III</td>
<td>Any T</td>
<td>N1</td>
<td>M0</td>
</tr>
<tr>
<td>Stage IV</td>
<td>Any T</td>
<td>Any N</td>
<td>M1</td>
</tr>
</tbody>
</table>

**Prognostic Factors Grid**
## Prognostic factors for survival for retinoblastoma

<table>
<thead>
<tr>
<th><strong>Prognostic factors</strong></th>
<th><strong>Tumour related</strong></th>
<th><strong>Host related</strong></th>
<th><strong>Environment related</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Essential</strong></td>
<td>Massive = ( \geq 3 \text{ mm} ) uveal invasion</td>
<td>Immunosuppression (i.e. AIDS) Germline mutation ( RB1 ) allele</td>
<td>Access to care</td>
</tr>
<tr>
<td>Extrascleral tumour extension</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Optic nerve invasion</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anterior chamber extension</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Higher UICC T category</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Additional</strong></td>
<td>Multidrug resistance gene(s)</td>
<td></td>
<td>Cyclosporine therapy</td>
</tr>
<tr>
<td>Heritability</td>
<td></td>
<td></td>
<td>Experienced multidisciplinary team (local control)</td>
</tr>
<tr>
<td><strong>New and promising</strong></td>
<td></td>
<td>Screening programmes for less developed countries</td>
<td>Telepathology for evaluation of enucleated eyes <em>In utero</em> detection of Rb</td>
</tr>
</tbody>
</table>


### Sarcoma of Orbit

(ICD-O-3 C69.6)

#### Rules for Classification

The classification applies to sarcomas of soft tissue and bone. There should be histological confirmation of the disease and division of cases by histological type.

The following are the procedures for assessing **T**, **N**, and **M** categories:

- **T categories**: Physical examination and imaging
- **N categories**: Physical examination
- **M categories**: Physical examination and imaging
Regional Lymph Nodes
The regional lymph nodes are the preauricular, submandibular, and cervical lymph nodes.

TNM Clinical Classification

T – Primary Tumour

TX Primary tumour cannot be assessed
T0 No evidence of primary tumour
T1 Tumour 20.0 mm or less in greatest dimension
T2 Tumour more than 20.0 mm in greatest dimension without invasion of globe or bony wall
T3 Tumour of any size with invasion of orbital tissues and/or bony walls
T4 Tumour invades globe or periorbital structure, such as eyelids, temporal fossa, nasal cavity and paranasal sinuses, and/or central nervous system

N – Regional Lymph Nodes

NX Regional lymph nodes cannot be assessed
N0 No regional lymph node metastasis
N1 Regional lymph node metastasis

M – Distant Metastasis

M0 No distant metastasis
M1 Distant metastasis

pTNM Pathological Classification

The pT and pN categories correspond to the T and N categories. For pM see page 8.

Stage

No stage is at present recommended.

Carcinoma of Lacrimal Gland

(ICD-O-3 C69.5)

Rules for Classification

There should be histological confirmation of the disease and division of cases by histological type.
The following are the procedures for assessing T, N, and M categories:

**T categories**  
Physical examination and imaging

**N categories**  
Physical examination

**M categories**  
Physical examination and imaging

### Regional Lymph Nodes
The regional lymph nodes are the preauricular, submandibular, and cervical lymph nodes.

### TNM Clinical Classification

**T – Primary Tumour**

- **TX** Primary tumour cannot be assessed
- **T0** No evidence of primary tumour

**T1** Tumour 2 cm or less in greatest dimension, with or without extraglandular extension into the orbital soft tissue
  - **T1a** No perosteal or bone involvement
  - **T1b** Periosteal involvement with out bone involvement
  - **T1c** Bone involvement

**T2** Tumour more than 2 cm but not more than 4 cm in greatest dimension, limited to the lacrimal gland
  - **T2a** No peristeal or bone involvement
  - **T2b** Periosteal involvement without bone involvement
  - **T2c** Bone involvement

**T3** Tumour more than 4 cm or with extraglandular extension into orbital soft tissue, including optic nerve, or globe
  - **T3a** No peristeal or bone involvement
  - **T3b** Periosteal involvement without bone involvement
  - **T3c** Bone involvement

**T4** Tumour invades adjacent structures (sinuses, temporal fossa, pterygoid fossa, superior orbital fissure, cavernous sinus, and/or brain)
  - **T4a** No more than 2 cm in greatest dimension
  - **T4b** More than 2 cm but no more than 4 cm in greatest dimension
  - **T4c** More than 4 cm in greatest dimension

**N – Regional Lymph Nodes**

- **NX** Regional lymph nodes cannot be assessed
No  No regional lymph node metastasis  
N1  Regional lymph node metastasis

M – Distant Metastasis

M0  No distant metastasis 
M1  Distant metastasis

pTNM Pathological Classification
The pT and pN categories correspond to the T and N categories. For pM see page 8.

Stage
No stage is at present recommended.
Hodgkin Lymphoma

Introductory Notes
The current staging classification for Hodgkin Lymphoma is a modification of the Ann Arbor classification first adopted in 1971. Over the past 45 years the practice has changed, making the previously used staging laparotomy and the resulting pathological staging classification obsolete. The recent consensus conference that took place in 2012 in Lugano suggested even more simplified system putting together stage I and II as Limited Stage and stage III and IV as Advanced Stage lymphoma. The Lugano Classification, a modification of the Ann Arbor classification, has been published and accepted by the UICC.¹

Clinical Staging (cS)
It is determined by history, clinical examination, imaging, blood analysis, and the initial biopsy report. Bone marrow biopsy must be taken from a clinically or radiologically non-involved area of bone.

Liver Involvement
Clinical evidence of liver involvement must include either enlargement of the liver and at least an abnormal serum alkaline phosphatase level and two different liver function test abnormalities, or an abnormal liver demonstrated by imaging and one abnormal liver function test.

Spleen Involvement
Clinical evidence of spleen involvement is accepted if there is palpable enlargement of the spleen confirmed by imaging.

Lymphatic and Extralymphatic Disease
The lymphatic structures are as follows:
- Lymph nodes
- Waldeyer ring
- Spleen
- Appendix
- Thymus
- Peyer patches
The lymph nodes are grouped into regions and one or more (2, 3, etc.) may be involved.
The spleen is designated S and extralymphatic organs or sites E.

**Lung Involvement**
Lung involvement limited to one lobe, or perihilar extension associated with ipsilateral lymphadenopathy, or unilateral pleural effusion with or without lung involvement but with hilar lymphadenopathy is considered as **localized** extralymphatic disease.

**Liver Involvement**
Liver involvement is always considered as **diffuse** extralymphatic disease.

**Clinical Stages (cS)**

**Limited Stage**

**Stage I**
Involvement of a single lymph node region (I), or localized involvement of a single extralymphatic organ or site (IE).

**Stage II**
Involvement of two or more lymph node regions on the same side of the diaphragm (II), or localized involvement of a single extralymphatic organ or site and its regional lymph node(s) with or without involvement of other contiguous lymph node regions on the same side of the diaphragm (IIE).

**Bulky Stage II**
Stage II disease with a single nodal mass greater than 10 cm in maximum dimension or greater than a third of the thoracic diameter as assessed on CT.

**Advanced Stage**

**Stage III**
Involvement of lymph node regions on both sides of the diaphragm (III), which may also be accompanied by involvement of the spleen (IIIS).

**Stage IV**
Disseminated (multifocal) involvement of one or more extralymphatic organs, with or without associated lymph node involvement; or non-contiguous extralymphatic organ involvement with involvement of lymph node regions on the same or both sides of the diaphragm.

**A and B Classification (Symptoms)**
Each stage should be divided into A and B according to the absence or presence of defined general symptoms. These are:

1. Unexplained weight loss of more than 10% of the usual body weight in the 6 months prior to first attendance
2. Unexplained fever with temperature above 38°C
3. Night sweats

Note

Pruritus alone does not qualify for B classification nor does a short, febrile illness associated with a known infection.

Reference

Non-Hodgkin Lymphomas

The Lugano classification, a modification of the Ann Arbor classification, is recommended as for Hodgkin lymphoma with the exception of the elimination of the A or B classification of symptoms (see page 237).

In Stage II disease, bulk is defined as larger than 6 cm in greatest dimension in follicular lymphoma, and 10 cm in largest dimension has been recommended for diffuse large cell lymphoma.
Essential TNM

Introductory Notes (see also page 13)
When the T, N, and M categories have not been recorded in the clinical records or if the data to determine the categories is not available, the cancer registrar can code the extent of disease according to the Essential TNM scheme. Using the schema for breast, colorectal, prostate, or cervical cancer (Figures 2, 3, 4, and 5), the extent of disease may be recorded as Stage I, II, III, or IV or if insufficient data as distant, regional, or localized.

Rules for Classification
Essential TNM is composed of three key elements that together summarize the extent of cancer in the patient:

M Presence or absence of distant metastasis
N Presence or absence of regional lymph node metastasis/involvement
T Extent of invasion and/or size of the tumour

Coding the Elements of Essential TNM

Metastasis (M)

M+. Presence of distant metastasis including non-regional nodes
M– No mention of distant metastases, clinically or pathologically

Regional Node Metastasis/Involvement (N)

R+. Presence of regional node metastasis/involvement
R– No mention of regional node metastases, clinically or pathologically

Extent of Invasion and/or Size of Tumour (T)
Depending on the information available, the T category can be recorded or if not available the extent of the local tumour as advanced or localized.

A Extent of invasion and/or tumour size is Advanced
A2 Extent of invasion and/or tumour size is very advanced
A1 Extent of invasion and/or tumour size is advanced
L Extent of invasion and/or tumour size is Limited
L2 Extent of invasion and/or tumour size is limited
L1 Extent of invasion and/or tumour size is very limited
Extent of invasion and/or tumour size cannot be assessed

Colon and Rectum Essential TNM
Figure 2 Colon and rectum essential TNM.
Breast Essential TNM

Figure 3 Breast essential TNM.

Cervix Essential TNM
Figure 4 Cervix essential TNM.
Figure 5 Prostate essential TNM.
Paediatric Tumours

Introductory Notes (see also page 13)
The classifications in this section are not intended to replace the classifications used by the clinician when treating an individual patient but to facilitate the collection of stage by population-based cancer registries. The consensus meeting held in 2014 recommended a tiered staging system with more detailed systems for well resourced cancer registries and less detailed systems for registries with limited resources and access; as with Essential TNM, lower tiered systems are based on collapsing higher tiered systems. The recommendations for tier 1 and 2 follow. Well resourced registries may choose to collect additional accepted prognostic factors such as those used in the clinical setting but these are not included in this section. For some cancers, recommendations are the same as described earlier for adult patients and the appropriate page number is given; others are referenced where appropriate. Rules for the derivation of paediatric cancer stage in population based cancer registries are being developed and will be available from the UICC website when available.

Rules for Classification
The classification applies only to paediatric malignant tumours.

Gastrointestinal Tumours

Hepatoblastoma
Tier 1 and 2
- Metastatic Distant metastases present
- Localized Tumour confined to the liver including regional lymph nodes
Well resourced cancer registries may wish to use the Pretext Classification.

Bone and Soft Tissue Tumours

Osteosarcoma
Tier 1 and 2
- Metastatic Distant metastases present
- Localized Tumour confined to area of origin including regional lymph nodes
Ewing Sarcoma

Tier 1 and 2

Metastatic Distant metastases present
Localized  Tumour confined to area of origin including regional lymph nodes

Rhabdomyosarcoma

Tier 1

Metastatic Distant metastases present
Localized  Tumour confined to the area of origin including regional lymph nodes

Tier 2

A modified TNM Clinical Classification with the addition of favourable or non-favourable tumour site.

T – Primary Tumour*

TX  Primary tumour cannot be assessed
T0  No evidence of primary tumour
T1  Confined to a single anatomic site
T1a  Tumour 5 cm or less in greatest dimension
T1b  Tumour more than 5 cm in greatest dimension
T2  Extension beyond anatomic site
T2a  Tumour 5 cm or less in greatest dimension
T2b  Tumour more than 5 cm in greatest dimension

N – Regional Lymph Nodes

NX  Regional lymph nodes cannot be assessed
N0  No regional lymph node metastasis
N1  Regional lymph node metastasis

M – Distant Metastasis

M0  No distant metastasis
M1  Distant metastasis

Note

* For the eighth edition in adults this has been revised (see page 124).
The prognostic grouping for rhabdomyosarcoma includes favourable anatomic sites and unfavourable anatomic sites.

**Favourable anatomic sites:** Orbit, head and neck (excluding parameningeal tumours) and genitourinary sites (excluding bladder and prostate tumours)

**Unfavourable anatomic sites:** Bladder, prostate, extremity, cranial, parameningeal, trunk, retroperitoneum and all other sites not noted as favourable

**Stage I**
Any T  
Any N  
M0  
Favourable Site

**Stage II**
T1a, T2a  
No  
M0  
Unfavourable Site

**Stage III**
T1a, T2a  
N1  
M0  
Unfavourable Site

**Stage IV**
Any T  
Any N  
M1  
Any Site

**Soft Tissue Sarcoma other than Rhabdomyosarcoma**

**Tier 1**

Metastatic Distant metastases present

Localized  Tumour confined to the area of origin including regional lymph nodes

**Tier 2**

The TNM Classification is recommended

See Classification for soft tissue sarcoma of the trunk and extremity on page 124 for definitions of T category and N category.

**Gynaecological Tumours**

**Ovary**

**Tier 1**

Metastatic Distant metastases excluding peritoneal metastases

Regional  Tumour extension to pelvis, peritoneum outside the pelvis, and/or retroperitoneal lymph nodes

Localized  Tumour confined to the ovaries (one or both)

**Tier 2**

Stage  Tumour confined to the ovaries (one or both)

Stage  Tumour extension to pelvis without extension to peritoneum outside the pelvis
nor to retroperitoneal lymph nodes

Stage III Tumour extension to peritoneum outside the pelvis and/or retroperitoneal lymph nodes

Stage IV Distant metastases present (excludes peritoneal metastases)

Note
* The UICC Stage Group corresponds to the FIGO stage.

Urological Tumours

Testes

Tier 1

Metastatic Distant metastases present
Regional Tumour extension to regional lymph nodes
Localized Tumour confined to the testes

Tier 2

See Classification for testes on page 195 for definitions of T category and N category. *

Stage I Any T N0 M0
Stage II Any T N1, N2, N3 M0
Stage III Any T Any N M1

Note
* For Tier 2 this is irrespective of serum tumour markers.

Well resourced cancer registries may wish to use the Classification on page 195 as used for adults that includes serum tumour markers.

Wilms Tumour

Tier 1

Metastatic Distant metastases present
Localized Tumour confined to the area of origin

Tier 2

Two Tier 2 staging classifications exist for Wilms Tumour. The classification of the Children’s Oncology Group/National Wilms Tumour Study Group (NWTS) is
utilized after surgical resection, prior to chemotherapy. The classification of the International Society of Paediatric Oncology (SIOP) is utilized if chemotherapy has been given preoperatively, prior to surgical resection.\cite{siop}

**Ophthalmic Tumours**

**Retinoblastoma**

**Tier 1**

- Metastatic Distant metastases present
- Regional  
  Orbital extension or regional lymph nodes
- Localized  
  Intraocular

**Tier 2**

This classification is determined after enucleation and is therefore a pathological classification.

**Prognostic Group**

- **Stage 0** The tumour is confined to the globe. Enucleation has not been performed
- **pStage I** Enucleation with negative margins (R0)
- **pStage II** Enucleation with microscopic residual disease (R1)
- **pStage III** Involvement of the orbit and/or metastases to regional lymph nodes
- **cStage IV** Metastatic disease

**Note**

Well resourced cancer registries may wish to use the Classification page 226 as used for adults.

**Malignant Lymphoma**

**Hodgkin Lymphoma**

See Classification on page 235.

**Non-Hodgkin Lymphoma**

**Tier 1**

- Advanced  
  Involvement of bone marrow and/or CNS
- Limited  
  No involvement of bone marrow or CNS
**Tier 2**

The St Jude/Murphy system is recommended\(^5\)

Stage Involvement of a single tumour mass or nodal area, excluding the mediastinum and abdomen

Stage Involvement of a single tumour mass with regional node(s) or two or more tumours and/or nodal regions on the same side of the diaphragm, or a completely resected primary gastrointestinal tract tumour with or without regional nodal involvement

Stage Tumour masses and/or regional nodes on opposite sides of the diaphragm or primary intrathoracic tumour (mediastinal, pleural or thymic) or extensive primary intraabdominal disease or paraspinal tumour or epidural tumour

Stage Involvement of bone marrow and/or central nervous system

**Central Nervous System**

**Medulloblastoma and Ependymoma**

**Tier 1**

Metastatic Disease beyond local site (e.g., other lesions in brain or spine, tumour cells in CSF or distant metastases)

Localized Localized disease

**Tier 2**

The classification is based on the extent of metastatic disease.\(^6\)

**Neuroblastoma**

**Tier 1**

MS Meta...


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