Standards and datasets for reporting cancers

Dataset for the histological reporting of testicular neoplasms

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NICE has accredited the process used by The Royal College of Pathologists to produce its Cancer Datasets and Tissue Pathways guidance. Accreditation is valid for 5 years from July 2012. More information on accreditation can be viewed at www.nice.org.uk/accreditation.

For full details on our accreditation visit: www.nice.org.uk/accreditation.
Foreword

The cancer datasets published by The Royal College of Pathologists (RCPath) are a combination of textual guidance, educational information and reporting proformas. The datasets enable pathologists to grade and stage cancers in an accurate, consistent manner in compliance with international standards and provide prognostic information, thereby allowing clinicians to provide a high standard of care for patients and appropriate management for specific clinical circumstances. It may rarely be necessary or even desirable to depart from the guidelines in the interests of specific patients and special circumstances. The clinical risk of departing from the guidelines should be assessed by the relevant multidisciplinary team (MDT); just as adherence to the guidelines may not constitute defence against a claim of negligence, so deviation from them should not necessarily be deemed negligent.

Each dataset contains core data items that are mandated for inclusion in the Cancer Outcomes and Services Dataset (COSD – previously the National Cancer Data Set) in England. Core data items are items that are supported by robust published evidence and are required for cancer staging, optimal patient management and prognosis. Core data items meet the requirements of professional standards (as defined by the Information Standards Board for Health and Social Care [ISB]) and it is recommended that at least 95% of reports on cancer resections should record a full set of core data items. Other, non-core, data items are described. These may be included to provide a comprehensive report or to meet local clinical or research requirements. All data items should be clearly defined to allow the unambiguous recording of data.

The following stakeholder organisations have been consulted during the preparation of the dataset:

- BAUS/BAUS Section of Oncology
- NCRI Testis Cancer Clinical Studies Group
- British Association of Urological Pathologists (BAUP)
- UK Association of Cancer Registries (UKACR).

Advice has also been sought from:

- International Society of Urological Pathology (ISUP)
- European Network of Uropathology (ENUP).

Evidence review

Evidence was sought by review of the previous dataset, CINAHL (Cumulative Index to Nursing and Allied Health) and PubMed searches reviewing recent articles on risk factors associated with testicular cancer. Recent review articles on testicular cancer were also reviewed. Strength of the data was assessed by the modified Scottish Intercollegiate Guidelines (SIGN) – see Appendix E.

Supporting evidence and recommendations in this dataset are also based on:

- PubMed literature searches (up to July 2013)
- WHO classifications, 1973 and 2004
- NICE Improving Outcomes Guidance, 2002

Most of the supporting evidence is level C or D at least or meets the GPP (Good Practice Point) criteria. Evidence is often poor for these relatively rare tumours, usually limited to large cohort studies at best. Disagreements between the authors were settled by discussion, and where no agreement was possible, this has been discussed in the text. No major conflicts in the evidence have been identified and any minor discrepancies between evidence have been resolved by expert consensus.
No major organisational changes have been identified that would hinder the implementation of the dataset and there are no new major financial or work implications arising from the implementation, compared to the previous dataset.

A formal revision cycle for all cancer datasets takes place on a three-yearly basis. However, each year, the College will ask the authors of the dataset, in conjunction with the relevant sub-specialty adviser to the College, to consider whether or not the dataset needs to be revised. A full consultation process will be undertaken if major revisions are required, i.e. revisions to core data items (the only exception being changes to international tumour grading and staging schemes that have been approved by the Specialty Advisory Committee on Cellular Pathology and affiliated professional bodies; these changes will be implemented without further consultation). If minor revisions or changes to non-core data items are required, an abridged consultation process will be undertaken, whereby a short note of the proposed changes will be placed on the College website for two weeks for members' attention. If members do not object to the changes, the short notice of change will be incorporated into the dataset and the full revised version (incorporating the changes) will replace the existing version on the College website.

The dataset has been reviewed by the Working Group on Cancer Services and was placed on the College website for consultation with the membership from 10 December 2013 to 10 January 2014. All comments received from the Working Group and membership were addressed by the authors to the satisfaction of the Chair of the Working Group and the Vice-President for Advocacy and Communications.

This dataset was developed without external funding to the writing group. The College requires the authors of datasets to provide a list of potential conflicts of interest; these are monitored by the Director of Clinical Effectiveness and are available on request. The authors of this document have declared that there are no conflicts of interest.

1 Introduction

Testicular cancer is the most common cancer in men under the age of 45. The majority of tumours are germ cell tumours, but there are numerous other types, making testicular tumours one of the most diverse areas of human pathology, despite their relative rarity. The picture is complicated by the post chemotherapy changes that are seen, as many tumours are treated by excision of residual disease, after metastasis has occurred. The National Institute for Health and Clinical Excellence (NICE) guidance, Improving Outcomes in Urological Cancer (www.nice.org.uk), recommended the establishment of a supra-network specialised testicular cancer multidisciplinary team, serving a population base of 2–4 million and managing 50–100 new patients a year. Patients with testicular cancer diagnosed by local urological multidisciplinary cancer teams should be referred to the specialist supra-network team and the diagnostic slides made available for review. It is expected that pathologists reporting testicular tumours and post-chemotherapy residual masses participate in the UK uropathology EQA scheme which includes testicular neoplasms.

The identification of pathological factors predictive of relapse in patients with disease apparently confined to the testis at presentation (clinical stage I) has meant that patients at low risk can be offered a range of options including surveillance, and for seminomas, adjuvant carboplatin is an increasingly popular option over radiotherapy in the UK.\(^1\) For patients with metastatic disease, international collaboration led to the development of an International Consensus Classification, based on the primary site, the presence and distribution of metastases and the level of the serum tumour markers alpha-fetoprotein (AFP), human chorionic gonadotrophin (hCG) and lactate dehydrogenase (LDH).\(^2\) This was subsequently adopted by the TNM classification system.\(^3\)

Patients presenting with metastatic disease and clinical or serological evidence of a germ cell tumour are referred for immediate chemotherapy without prior orchidectomy because of the
very rapid doubling times of germ cell tumours. However, in the absence of a testicular lesion, biopsy may be required to differentiate between a germ cell tumour and other tumour types.

Due to the rarity of testicular tumours, there are few randomised, large-scale, international studies of prognosis and outcome, especially in low-risk tumours. The favourable outcome of most cases means that thousands of cases may be required to power a study sufficiently, and often multivariate studies are inadequate. These guidelines are therefore based on papers with large numbers of patients, often in the context of randomised clinical trials. The evidence for the importance of histopathological features in the management of patients with germ cell tumours has changed somewhat over the past ten years, and the TNM classification currently does not adequately reflect the information required by many oncologists for patient treatment. These guidelines therefore reflect best clinical practice in the United Kingdom.

There are changes within this third edition of the dataset compared with the second edition, published in 2007, to reflect changing clinical practice including the tendency for the use of surveillance in many patients rather than adjuvant therapy in stage I testicular germ cell tumours (especially in classical seminoma). This third edition evaluates the core data items for seminoma and non-seminomatous germ cell tumours separately, which is a change from the previous dataset, to reflect the different prognostic factors in these two tumour groups. Finally, the use of the WHO 2004 classification system for testicular tumours is made mandatory and use of the BTTP (British Testicular Tumour Panel) classification system in addition to this is discouraged, in order to align the UK with other countries.

**Target users and health benefits of this guideline**

Although the supra-network model of testicular tumours is now well developed, it should be remembered that testicular cancers are usually diagnosed in local hospitals prior to referral to specialist centres. The target primary users of the dataset are trainee and consultant cellular pathologists and, on their behalf, the suppliers of IT products to laboratories. The secondary users are surgeons and oncologists, cancer registries and the National Cancer Intelligence Network. Standardised cancer reporting and multidisciplinary team (MDT) working reduce the risk of histological misdiagnosis and help to ensure that clinicians have all of the relevant pathological information required for tumour staging, management and prognosis. Collection of standardised cancer specific data also provides information for healthcare providers, epidemiologists, and facilitates international benchmarking and research.

The health benefits of conformity to the guidelines and reasons for adoption include:

- subtyping and staging of testicular tumours to determine subsequent clinical management and follow-up
- consistent reporting of pathological risk factors, which vary depending on the tumour subtype and clinical context, to allow patients to make informed decisions about their care
- adoption of a consistent approach to classification and risk assessment of testicular cancers, which is essential for audit and epidemiological studies.

2 **Clinical information required on the specimen request form**

Laterality, the type of specimen (biopsy, simple or radical orchidectomy, lymphadenectomy or post-chemotherapy residual mass), the anatomical origin of lymph nodes and history of prior testicular tumours and treatment should be stated. Information concerning serum tumour markers is extremely helpful and should be encouraged locally. It is hoped that the tumour markers (LDH, AFP, βhCG) should always be available at the time of surgery in all cases of suspected neoplastic disease of the testis. For lymphadenectomies, further clinical information such as the side of resection or type of resection (template or removal of specific
lesion) and also orientating sutures are helpful to allow correlation with the radiological findings. Unlike in lymph node dissection specimens from other sites, there is no requirement for identifying any specific prognostic nodes, such as an apical node.

3 Preparation of specimens before dissection

Specimen types include the following:
- radical orchidectomy
- testicular biopsies
- partial orchidectomy
- lymph node excision
- removal of other metastatic lesions (liver, lungs, brain).

3.1 Request forms/tracking

Appropriate labelling of request forms and containers must be observed by the requesting clinical team to avoid delays in the booking in of specimens. If available, specimen tracking with bar coding should enable the progress of specimens to be followed during transport and processing in the laboratory, which would help auditing of turnaround times for reporting.

3.2 Tissue fixation

- Orchidectomy and lymphadenectomy specimens generally require fixation in formalin for 24 hours. Fixative can be slow to penetrate the thick testicular coverings, therefore careful incision into the capsule is extremely helpful for tumour preservation. Although this should ideally be done by the pathologist, it is recognised that delay in incision can lead to poor tissue preservation, which may compromise the most important part of the assessment of testicular tumours (tumour typing). This should be performed by opening the tunica vaginalis (membranes) and slicing through the lateral border of the testis, cutting towards the epididymis.

- In some centres, surgeons have been educated in careful ‘bivalving’ of the fresh specimen. This can lead to bulging of the cut surfaces and the distortion can make assessment of the relationship between the tumour and tunica difficult. However, the authors consider that this is less important than compromising on tumour type assessment. Because germ cell tumours are particularly poorly cohesive (especially if poorly fixed), there may also be artefactual contamination of relevant resection margins, which should not be mistaken for direct stromal or vascular invasion.

- Biopsies or partial orchidectomies are unlikely to require incision before fixation as they are smaller and formalin penetrates them well. For partial orchidectomies, this should also be discouraged as surgical margins are of paramount importance. Depending upon personal preference and experience, biopsies may be fixed in Bouin’s solution for fertility studies to preserve nuclear morphology.

4 Specimen handling and block selection

A synoptic reporting proforma has been added as an aide memzire for the main features of these neoplasms (Appendices C and D). The proforma extracts the dataset currently used in diagnosis and staging. This is usually supplemented by a more detailed written report. Aspects of best practice in handling testicular tumour specimens have recently been reviewed as part of larger articles on testicular practice.4-6
4.1 Orchidectomy specimens

Most patients with a clinical diagnosis of testicular tumour undergo a radical orchidectomy, whereby the testis is removed with the tunica, epididymis and a length of spermatic cord via an inguinal approach. Partial orchidectomies may be performed in very specific circumstances, often when the contralateral testis has already been removed, to preserve endocrine function and the potential for natural reproduction. Excision margins or the testicular parenchyma should be inked in these cases. Subcapsular orchidectomies are now rarely performed in the context of prostate cancer. Simple orchidectomies, usually for benign disease, involve the removal of the testis, epididymis and a very short segment of cord via the scrotum. Radical testicular specimens should be orientated by identifying the cord, the slightly more bulbous head of epididymis tapering to the tail of the epididymis, separated from the testis proper by the epididymal sinus.

The testis should be measured in three dimensions and the length of spermatic cord recorded. The terms of proximal and distal are best avoided when referring to the cord, as they can cause confusion. A block is taken by the pathologist from the cord resection margin and, although some have suggested that this block is taken prior to incision of the tumour to avoid contamination, contamination of the cord margin is rarely a significant issue. It is preferable to rapidly bivalve and fix the testis before the cord margin block is taken to facilitate good fixation and accurate histological assessment of tumour type. If not already performed, the tunica vaginalis (TV) is opened and the testis sliced through the lateral border of the testis, cutting towards the epididymis. The parietal TV can then be reflected and the presence of a hydrocoele and/or adhesions noted. Especially for small tumours, it is necessary to thinly slice the residual testis tissue parallel to this, or some pathologists prefer to slice the remaining tissue into 4 mm slices in the horizontal plane, which allows the relationship between the tumour and the rete testis and the tumour and the tunica to be seen clearly.

While some take sections from the midpoint of the cord, we do not believe that this is mandatory unless a macroscopic abnormality is seen. However, macroscopic examination of the cord to look for abnormalities is necessary in all cases. There is evidence that vascular invasion is not seen in the cord unless it is also present adjacent to the main tumour, therefore it appears unnecessary to perform major blocking of the cord for little additional useful information. Direct invasion into the cord should be noted for staging purposes (pT3). Section(s) should be taken of the base of the cord to determine if there is microscopic invasion or to confirm macroscopic invasion. No clear criteria for T3 disease have been suggested in the literature and the authors have debated whether the peri-testicular adipose tissue present adjacent to the epididymis should be included as cord or whether T3 disease should be restricted to the fat between the testis head and the cord margin above the insertion of the TV. This lacks an evidence base, and clearly this is controversial internationally with expert opinions ranging from hilar fat invasion representing either of pT1, pT2 or pT3. Until there is international consensus on this issue and/or further evidence emerges, we suggest that either scenario is considered pT3 (i.e. the hilar fat is considered part of the spermatic cord), but with a description in the text of the report as to the reason for this staging. This follows the guidance in a TNM ‘frequently asked question’ document. This is a view supported by a recent paper showing the poor prognosis of peri-testicular hilar fat invasion in non-seminomas.

The authors also considered the staging of soft tissue deposits in the cord that were separate from the main testicular tumour and non-contiguous (which is a rare occurrence). This has only been studied in one abstract and suggests it is strongly associated with vascular invasion, and is better regarded as a soft tissue deposit (metastasis) rather than direct invasion of the cord and staged as pT2. A stage of pT3 is reserved for direct invasion of the cord only. This has been confirmed by the TNM helpdesk.

We also note there is some variation by pathologists in what is regarded as the definition of TV invasion. While many expert testicular pathologists regard invasion of the outer serosal
layer of the testis as defining of TV invasion, in fact both serosal layers constitute the TV (and should be considered pT2), while the tunica albuginea is merely the bland fibrous tissue under the serosa. The evidence behind the utilisation of TV invasion (however defined) as a risk factor for recurrent disease is absent, however, and we believe this is an issue with the current TNM classification. For practical purposes, invasion of the outer (parietal) TV can be noted macroscopically and invasion of the inner (visceral) TV can be seen microscopically, but we believe that while it is necessary to be cognisant of the TNM classification, TV invasion should not change treatment options in clinical scenarios.

In summary, the following are noted:

- tumour location (upper pole, mid section or lower pole)
- the appearance (solid or cystic) and colour of the tumour
- the maximum tumour size
- multifocality, if present
- the relationship of the tumour to the tunicae, rete (if identifiable), epididymis and cord
- the presence of abnormalities in the residual normal testis.

4.2 Primary lymphadenectomy specimens

Although retroperitoneal lymph node dissections can be performed as an alternative to surveillance or chemotherapy in patients with stage I disease, this is unusual in the UK. Any such specimens are measured in three dimensions. Lymph nodes are identified and described as either macroscopically normal or involved by tumour. The size of any lymph node masses should be noted as this is required for TNM staging. Inking for margins is recommended.

4.3 Excision of residual masses after chemotherapy

A complete (template) retroperitoneal lymph node dissection may be performed in many cases, but sometimes only the involved lymph nodes are removed ('lumpectomy'). Specimens are measured in three dimensions. The size of any lymph node masses should be noted as this is required for TNM staging. It is recommended to ink surgical resection margins, as completeness of excision is a determinant of outcome. The masses usually consist of single or multiple lymph nodes, but occasionally visceral metastasis may be resected.

4.4 Block selection

Comprehensive sampling is essential for both primary resections and residual masses, as the identification of even a small area of a different subtype can alter patient management and impact on prognosis. Although the recommendation of one block per centimetre of tumour is usual, more may be required to adequately represent all the macroscopically different areas of tumour as well as the interface with surrounding structures for staging and management purposes. Large seminomas may harbour small areas of non-seminoma, which changes the management of the patient. Very thorough blocking of macroscopic seminomas is suggested.

**Orchidectomy specimens for clinically localised disease**

Blocks are selected to represent:

- the cord resection margin and base of cord (further cord blocks depending on macroscopy)
- the relationship of the tumour(s) to the rete testis, epididymis and cord
• the minimum distance of the tumour to the nearest inked resection margin for partial orchidectomies
• all areas of the tumour(s) with different macroscopic appearances (solid, cystic, pale or haemorrhagic)
• adjacent testis including the capsule, a common site for vascular invasion
• uninvolved testis.

**Retroperitoneal lymph node dissections and post-chemotherapy residual masses**

Blocks are selected to represent:
• all areas of the positive node(s) with different macroscopic appearances (solid, cystic, pale or haemorrhagic)
• the minimum distance of the tumour to the nearest resection margin (which may be inked)
• all macroscopically negative nodes to search for micrometastatic disease.

For post-chemotherapy residual masses, particularly in the absence of a biopsy diagnosis prior to treatment, it is often useful to include areas of necrosis, as ghost outlines of the tumour often remain and allow the distinction between seminoma and non-seminomatous germ cell tumour. It is important to recognise that residual viable malignancy (embryonal carcinoma, yolk sac tumour, classical seminoma or choriocarcinoma) may trigger further chemotherapy and therefore it is important to only report viable elements and not semi-viable or non-viable tumour. Necrosis and post chemotherapy teratoma would not usually trigger further therapy, unless the clinical situation dictates otherwise. For post-chemotherapy RPLND, it may be desirable to embed the entire specimen if the specimen is found to contain necrosis or non-viable tumour only to exclude a small focus of viable tumour.

5 **Core data items**

This is an evidence-based list of items that are essential for prognosis or management.

5.1 **Clinical data items:**

• type of specimen and procedure
• anatomic site

These items are self explanatory. Ideally serum makers would be a core data item, however during the consultation phase many pathologists highlighted the potential difficulty with obtaining these at the time of reporting. There are also occasional testes removed for trauma which have incidental germ cell tumours. This has therefore been removed as a core data item, but, knowledge of serum markers is desirable for optimal assessment of a tumour. For example, it is important to closely inspect and possibly more widely sample a case that appears macroscopically to be seminoma but in which there is a raised AFP. Identification of an additional non-seminomatous component will influence clinical management.

5.2 **Macroscopic data items:**

• number, location and description of tumour(s)
• maximum tumour dimension
• status of tunica vaginalis.

The first two items are unchanged from the previous dataset, except it has been clarified that it is the maximum tumour dimension which appears to have prognostic significance,
especially in seminomas. The status of the tunica vaginalis has been added though, as mentioned above, although it is essential for TNM staging, we cannot find evidence that it is a prognostic factor.

5.3 Microscopic data items

General points

The discussion below is split between seminoma and non-seminomatous germ cell tumours, as different prognostic factors appear important for these tumours, not all of which are in current staging or typing criteria. We considered producing two datasets, one for seminoma and one for non-seminomatous tumours, but felt this would be cumbersome, unwelcome and provide extra levels of complexity. We therefore recommend that core data items that have shown to be significant for seminoma or non-seminomatous germ cell tumours should be regarded as core data items for both groups. This does inflate the number of core data items, but avoids the complexity of a ‘split’ system. The authors believe that the TNM system is in need of major modification and clarification to assist clinical practice. Until this is performed, the dataset will remain somewhat cumbersome.

5.3.1 Classification

Accurate typing of a testicular tumour is of paramount importance and influences clinical decisions far more than pathological stage. The WHO 2004 system is used in virtually every country except the UK. The situation is complicated in the UK by the use of an alternative classification: the British Testicular Tumour Panel (BTTP) Classification. The BTTP system has not undergone any revision for 30 years and has not kept pace with the development of novel prognostic factors and new entities in testicular pathology. Although some oncologists still use the BTTP system, the vast majority now use the WHO system. Research studies are increasingly international, including in the field of testicular pathology where tumours are rare.

The authors strongly feel that while we owe a debt of gratitude to the authors who formulated BTTP, it should now be mandatory to classify by WHO 2004. Although pathologists have the option to use BTTP if locally requested, we do not think this should be encouraged, as it now puts the UK out of step with virtually every other country. There is also potential for confusion when discussing cases with clinical colleagues (e.g. ‘teratoma’ or MTU, which may be either yolk sac tumour or embryonal carcinoma) when switching between the two systems. However, in reality, both systems have many similarities and recognise that the main division of germ cell tumours is between seminomas and non-seminomatous germ cell tumours.

5.3.2 Classical seminoma

Approximately 50–55% of germ cell tumours are currently pure seminoma. There are two types of seminoma: classical seminoma and spermatocytic seminoma. Spermatocytic seminoma is much less common than the classical type, almost never metastasises and orchidectomy alone is standard management. These appear separate from other germ cell tumours on genetic as well as morphological grounds.

In comparison to NSGCT, there is less literature and information available about prognostic factors in seminoma, probably due to the lower rates of recurrence and death, making studies extremely hard to power statistically. Current management practice is for surveillance in the majority of patients with stage I classical seminoma and has been used in some centres for over 30 years. If adjuvant therapy is the patient’s or oncologist’s preference, then adjuvant carboplatin is now generally the treatment of choice rather than radiotherapy, although this is disputed in some countries, notably the USA. Those with relapse are almost invariably salvaged by cisplatin-based chemotherapy. Death from stage I seminoma is extremely rare; a recent systematic review showing cause specific survival of
Almost all patients with stage I seminoma are cured, regardless of management strategy adopted after orchidectomy, and therefore any decisions about the need for adjuvant therapy in stage I seminoma should be made with the aim of reducing morbidity and recurrence risk, rather than mortality.

**Tumour size**

In a pooled analysis of data from four large cohort studies (638 patients), size (tumour size >4 cm) and rete testis invasion were the only two factors independently predictive of recurrence at five years on multivariate analysis. If the tumour was >4 cm, there was a two-fold increased risk of recurrence. Patients with both rete testis invasion and a tumour >4 cm were 3.4 times more likely to relapse than patients with no adverse factors.

*Level of evidence – C.*

**Tumour subtypes**

The recognition of ‘anaplastic seminoma’ with a possible worse prognosis remains controversial. It is clear that the original criteria, based on the mitotic rate of seminomas, is not effective in recognising aggressive behaviour. Often, tumours classified as ‘anaplastic seminomas’ are either poorly fixed seminomas, with obscuring of the diagnostic features, or solid pattern embryonal carcinomas. ‘Seminoma with atypia’ was described based on nuclear pleomorphism and crowding, dense cytoplasm and few lymphocytes. Such tumours were more likely to express CD30 and lose c-kit reactivity; we interpret this as likely early transformation to non-seminoma (embryonal carcinoma).

Small case series and individual case reports of an ‘anaplastic variant’ of spermatocytic seminoma have been described where there is a predominance of the intermediate size cells and a high mitotic index, but this does not seem to correspond to an adverse prognostic in the limited literature available and no patients have shown metastasis. There is therefore no evidence that tumours with this morphology display anything other than the almost invariably excellent prognosis of spermatocytic seminoma and use of this term is therefore not recommended.

**Invasion of the rete testis**

Although not included in the TNM staging system, in a pooled analysis of data from four large cohort studies, rete testis invasion was independently predictive of recurrence at five years on multivariate analysis, conferring an increased risk of recurrence by a factor of 1.7 (95% CI 1.1–2.6). This was confirmed by a further large cohort analysis of 425 patients. Rete testis invasion was defined in the pooled analysis as extension of tumour into the testicular mediastinum without necessarily involving the tubular lumens (i.e. rete testis stroma invasion only was counted and not pagetoid spread into the rete epithelium). Rete testis invasion should be specified as stromal invasion (core data item) or pagetoid spread into the epithelium of the rete (non-core data item).

At present, there is no evidence that pagetoid spread alone is a prognostic factor and many of these cases probably reflect intratubular germ cell neoplasia. We recognise that rete testis invasion and tumour size are probably closely related and further work may show which is superior in multivariate analysis. Smaller recent series have not confirmed that rete testis invasion is an independent predictor of progression. However, currently, both are used by many clinicians to determine adjuvant chemotherapy and are part of existing clinical guidelines. The failure to discriminate between rete testis stroma invasion and pagetoid spread in some studies can make it difficult to draw meaningful conclusions.

*Level of evidence – C.*
Direct invasion of the cord

This is regarded as a core data item as it is required for TNM staging but evidence on its prognostic significance in seminoma is lacking. In a large cohort study of stage I seminoma, spermatic cord invasion was not found to be independently prognostic for recurrence. In a review of 326 testicular germ cell tumours, of which 79 had tumour in the spermatic cord, most cases (72%) were thought to be due to contamination compared to 19% cases of true involvement and with 8.9% showing both contamination and true involvement. Spermatic cord contamination was most frequently seen with seminomas. Because of the extremely friable nature of seminoma, careful specimen handling and interpretation is required. The definition of cord invasion has been discussed in macroscopic assessment.

[Vascular (lymphatic and/or venous) invasion

Although lymphovascular invasion has been shown to be a statistically significant factor predicting for relapse in occasional small cohort studies, it has not proved independently statistically significant in stage I seminoma in large cohort pooled studies. The lack of statistical significance may be because of the frequent presence of tumour smearing artefact in seminoma, making identification of genuine lymphovascular invasion challenging. Lymphovascular invasion is a core data item for classical seminoma as it is part of the TNM staging system, but will not necessarily inform treatment decisions.

At present, there is no evidence for the introduction of the routine use of immunohistochemistry such as D2-40 against podoplanin (identification of lymphatic endothelium) or CD34 (vascular endothelium) to assist in identifying lymphatic or vascular invasion, although this may help in individual cases. CD34 is present in normal testicular stroma. It is not possible to state with certainty whether it is a blood vessel or lymphatic invasion in many instances.

Lymphovascular invasion may be seen in the tunica albuginea, spermatic cord vessels or the parenchyma of the testis. All warrant a stage of pT2. Its presence in spermatic cord vessels does not warrant a stage of pT3 and this should be staged as pT2 even if there is invasion of the tumour out of the vessels into the cord soft tissue, as this represents a soft tissue deposit of tumour.

[Level of evidence for lymphovascular invasion – D.]

Other factors

DNA ploidy status, mitotic rate, DNA S phase percentage, gene expression analysis of genes such as DRD1 or FAM71F2, the presence of syncytiotrophoblastic giant cells, the degree of lymphocytic infiltrate in the tumour, expression of β-hCG, low molecular weight keratins, p53, Ki67, CD30 or loss of CD117 expression on immunohistochemical analysis, spontaneous regression or necrosis have been studied to identify patients at risk of recurrence or metastasis, but at present significant evidence on any of these as a predictor of recurrence/metastasis is either limited or absent.

5.3.3 Non-seminomatous germ cell tumours (NSGCT)

Vascular invasion

Unlike seminomas, lymphovascular invasion is the most powerful prognostic factor for stage I NSGCT. In a study of 102 men with stage I NSGCT, Fosså et al. showed that lymphovascular invasion was the most significant risk factor predicting relapse (p=0.0007).
In a separate study, lymphovascular invasion was also identified as a significant poor prognostic factor, where 62% of men with lymphatic invasion developed distant metastases. This is further confirmed by Colls et al., where they demonstrated that 46% of men with vascular lymphatic invasion in their primary tumour experienced relapse. In an evaluation of 88 stage I NSGCTs, multivariate analysis showed that 23 of 88 patients with vascular invasion of the primary tumour had a high risk of relapse (61%, 95% CI 55–67%) and a linked cohort, surveillance of 105 men with stage I NSGCTs revealed that 27/105 (25.7%) men had disease relapse. All relapses in this group of men occurred within two years of orchidectomy and vascular invasion was identified as one of the significant predictors of relapse during surveillance. Further, in examining the records of 82 patients with stage I NSGCTs following radical orchidectomy, 30 of 82 patients did not have vascular invasion in their primary tumour, whereas 52 of 82 men had vascular invasion. In the group of men who had vascular invasion, 24 of 52 (46%) experienced relapse, thus indicating that vessel invasion could be used as a prognostic factor in monitoring stage I NSGCTs. If lymphovascular invasion is present in a mixed or combined germ cell tumour, it is good practice to state which subtype of tumour is showing the lymphovascular invasion as this may alter clinical management if it was an embryonal carcinoma component showing lymphovascular invasion versus classical seminoma. Indicating that a case is 'uncertain' for vascular invasion is unhelpful for the treatment of patients with germ cell tumours. It is suggested that vascular invasion is noted as positive in cases where the pathologist is certain of its presence and called negative when features are equivocal.

*Level of evidence for lymphovascular invasion – C.*

**Percentage of embryonal carcinoma**

The percentage and volume of embryonal carcinoma is another prognostic factor associated with the rate of relapse in stage I NSGCTs. In a study of 132 patients, the presence of lymphovascular invasion, embryonal carcinoma and yolk sac tumour were risk factors for relapse. Another study showed that 25/85 men who had predominantly embryonal carcinoma histology relapsed (p=0.008). Of 93 men with stage I NSGCTs who were placed in a surveillance study following orchidectomy, 81 men had predominantly embryonal carcinoma component in their primary tumour and a third of these developed metastases, whereas none of the men lacking an embryonal carcinoma component developed metastases (p=0.05). A surveillance study in 373 men with stage I NSGCT suggested that ‘undifferentiated cells’ and the absence of yolk sac elements in the primary tumour were able to identify men with a high risk of relapse. It is helpful for clinicians to know the approximate proportions of each tumour subtype present, so in addition to giving the percentage of embryonal carcinoma as a core data item, the approximate percentages of other tumour elements should also be given.

*Level of evidence for percentage of embryonal carcinoma – C.*

**Invasion of the rete testis**

This is a core data item for non-seminomatous germ cell tumours as it is a core data item for seminoma. Also, there is limited evidence that it is associated with advanced clinical stage at presentation.

*Level of evidence – D.*

**Somatic transformation**

Rarely, a teratoma can show malignant overgrowth of either sarcoma, carcinoma or PNET (overgrowth of immature neuroepithelium). An evidence base for a definition of overgrowth is lacking, but in PNET and sarcoma, it is usually considered as involvement of one low-power (x4) field. Overgrowth by somatic carcinoma is characterised by invasive growth.
Tumour stage

Other groups have also identified additional histopathological adverse prognostic predictors of relapse for stage I NSGCTs. These include spermatic cord involvement (T3 disease)\textsuperscript{11,48} and scrotal invasion (T4).\textsuperscript{46} These features are incorporated into the staging system yet few studies have validated the value of T3/T4 disease classification. As discussed previously, the definition of T3 disease is not well defined but, in view of the recent study that showed a poor prognosis related to direct hilar fat invasion, we suggest that this feature is routinely recorded.\textsuperscript{11}

Molecular studies

A number of studies have tried to investigate other factors of poor prognosis in NSGCTs but none has been clinically validated.\textsuperscript{49-52}

5.3.4 Intratubular germ cell neoplasia, unclassified (IGCNU)

IGCNU, also known as ‘carcinoma in situ’ and ‘testicular intratubular neoplasia’, is now recognised as the premalignant lesion of invasive germ cell tumours. Although not a prognostic factor, we recommend it should be a core item, as its absence may raise the suspicion of a non-germ tumour mimicking a germ cell tumour or the possibility of a dermoid cyst as opposed to a pure teratoma. Recognition of some of the tumour mimics of seminoma is difficult and the lack of IGCNU, especially in a seminoma, should alert the pathologist to the possibility of tumours with a very different natural history: notably spermatocytic seminomas or Sertoli cell tumours.\textsuperscript{53,54}

5.3.5 Non germ cell tumours of the testis

The assessment of non-germ cell tumours of the testis is highly specialised and challenging even for experts in the field. Most will be Leydig cell tumours and behave in a benign manner and need no follow up. However, some may be associated with clinical syndromes and rarely behave in a malignant fashion. Features suggestive of malignancy include invasion of other structures, lymphovascular invasion, large size, necrosis and increased mitotic activity. We recommend that if suspicious features are identified, referral to a national or even international expert is advised. Treatment of malignant cases may include a prophylactic retroperitoneal lymph node dissection.\textsuperscript{55} Lymphomas should be referred to a lymphoreticular expert.

5.4 Lymph node excisions

The role of pathology in metastatic disease is to confirm the diagnosis of a germ cell tumour if there is clinical uncertainty. However, prognosis and treatment decisions are then largely based on the International Consensus Classification.\textsuperscript{2} Serum markers and imaging are used to assess response to chemotherapy. Residual masses may persist after completion of treatment. Patients with seminoma do not generally require resection of a persistent mass, as the presence of residual viable seminoma and the development of recurrence are rare. On the other hand, in patients with non-seminomatous germ cell tumour, two thirds of resections contain viable disease, and it is not always possible to identify preoperatively those with fibrosis or necrosis only. It is only viable and not semi-viable or non-viable tumour elements that are clinically important. In some cases, it is not entirely straightforward to determine if tumour elements are viable or semi/non-viable. Features that might suggest the tumour is semi/non-viable are pyknotic nuclei, loss of cytoplasm and a degenerate appearance. The presence of germ cell elements other than teratoma, seen in 20–30% of cases, and incomplete resection are independent risk factors for progression.\textsuperscript{56} The presence of embryonal carcinoma has been identified as the single most significant risk factor for progression in patients with complete resections.\textsuperscript{57,58}
Transformation to other types of tumour is extremely difficult to assess and where there is doubt, referral to an expert in the area is recommended. Determination of whether there is extra-nodal spread of tumour should be stated, as this is required for nodal staging.

**Microscopic core data items for orchidectomy specimens:**
- tumour subtype(s)
- percentage of embryonal carcinoma and other tumour elements for all mixed tumours
- maximum tumour dimension (if not assessed macroscopically) (mm)
- invasion of the rete testis *stroma*
- direct invasion of the hilar soft tissue or cord (both considered pT3)
- lymphovascular invasion (lymphatic and/or venous invasion) and in mixed tumours, which tumour element shows lymphovascular invasion
- surgical margin status (partial orchidectomies)
- cord margin status (radical orchidectomies)
- presence or absence of intratubular germ cell neoplasia, unclassified (IGCNU)
- primary tumour categories (pT stage).

**Microscopic core data items for lymphadenectomies or resections of residual masses:**
- tumour subtype(s) and percentages
- viability of the tumour(s)
- margin status
- extranodal spread of tumour.

6 **Non-core data items**
- Pagetoid spread of seminoma/IGCNU into the rete testis epithelium.
- Epididymis invasion.
- Presence of normal spermatogenesis.

7 **Diagnostic coding and staging**

7.1 **TNM classification**

The 7th edition of TNM should be used\(^3\) (see Appendix A).

7.2 **Diagnostic coding**

Coding is recommended and is important for data retrieval, workload measurement and audit.

The site, histological diagnosis and procedure should be coded using SNOMED (Appendix B) or SNOMED-CT.

Procedure codes (P) are used in SNOMED 2 and SNOMED 3 to distinguish biopsies, partial resections and radical resections to indicate the nature of the procedure. Local P codes should be recorded. At present, P codes vary according to the SNOMED system in use in different institutions (Appendix B).
8 Reporting of biopsy specimens

Biopsy specimens are rarely received from testes in the setting of a suspected germ cell tumour as radical (or as a minimum partial) orchidectomy is standard management. There should be a very low threshold for performing additional immunohistochemical studies on testicular biopsies taken for suspected malignancy or if there is a history of, for example, maldescent. OCT3/4 staining is invaluable in highlighting subtle IGCNU or intertubular classical seminoma.

9 Reporting of frozen sections

Frozen sections for testicular neoplasms are difficult and produce a number of challenges. We believe that there is no role for testicular frozen section when a total orchidectomy has already been planned or when tumour markers strongly suggest a germ cell neoplasm. The main role for frozen section may be in the assessment of partial orchidectomy specimens, especially in men with a previous contralateral orchidectomy. A sex cord stromal tumour may be identified and prevent the need for a radical orchidectomy. Similarly, confirmation of a germ cell tumour may lead to a change to total orchidectomy. There are numerous potential pitfalls in the assessment of frozen section material in testicular neoplasms and for most pathology departments it is an unnecessary procedure, especially given the rarity of testicular tumours. Not least, the benign epidermoid cyst may be almost impossible to separate from a mature teratoma on frozen sectioning.

10 Use of immunohistochemistry/molecular tests

Immunohistochemistry can be used as an adjunct in confirmation of tumour types/subtypes, but is not necessary in most cases. It is particularly useful in settings such as confirming a tumour to be a germ cell tumour rather than another type of tumour such as lymphoma or sex cord stromal tumour, confirming a germ cell tumour subtype (e.g. seminoma versus solid pattern embryonal carcinoma or spermatocytic seminoma) or confirming the various elements present within a mixed germ cell tumour (e.g. yolk sac tumour versus embryonal carcinoma).

Some centres are able to offer isochromosome i(12p) FISH testing which, although not entirely specific, may be a useful additional test in confirming a tumour as a germ cell tumour. It is useful in some specific settings such as dermoid cyst of the testis (absence of i(12p)) versus teratoma (i(12p) in many cases).

11 Criteria for audit of the dataset

Recommended by the RCPath as key performance indicators (KPIs) (see Key Performance Indicators – Proposals for implementation (July 2013) on www.rcpath.org/clinical-effectiveness/kpi/KPI):

- Cancer resections must be reported using a template or proforma, including items listed in the English COSD which are, by definition, core data items in RCPath cancer datasets. English Trusts are required to implement the structured recording of core pathology data in the COSD by January 2014.
  
  Standard: 95% of reports must contain structured data

- Histopathology cases that are reported, confirmed and authorised within seven and ten calendar days of the procedure.

  Standard: 80% of cases must be reported within seven calendar days and 90% within ten calendar days.
References


30. Vogt AP, Chen Z, Osunkoya AO. Rete testis invasion by malignant germ cell tumor and/or intratubular germ cell neoplasia: what is the significance of this finding? *Hum Pathol*, 2010; 41:1339–1344.


Colls BM, Harvey VJ, Skelton L, Frampton CM, Thompson PI, Bennett M et al. Late results of surveillance of clinical stage I nonseminoma germ cell testicular tumours: 17 years' experience in a national study in New Zealand. *BJU Int* 1999;83:76–82.


Appendix A    TNM pathological staging (7th edition, UICC)

The classification applies only to germ cell tumours of the testis. The assessment of the serum tumour markers alpha-fetoprotein (AFP), human chorionic gonadotropin (hCG) and lactate dehydrogenase (LDH) contributes to the staging. Although pathologists may not be aware of specific levels to allow stage grouping, the details are provided here for information.

pT    Primary tumour

pTx    Primary tumour cannot be assessed (used if no radical orchidectomy has been performed, except for pTis and pT4, where radical orchidectomy is not always necessary for classification purposes).

pT0    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.

In the case of multiple tumours, the tumour with the highest T category should be classified and the multiplicity or number of tumours should be indicated in parentheses, e.g. pT2 (m) or pT2 (5).

pN    Regional lymph nodes

The regional lymph nodes are the abdominal para-aortic (peri-aortic), pre-aortic, interaortocaval precaval, paracaval, retrocaval, and retro-aortic nodes. Nodes along the spermatic vein should be considered regional.

Laterality does not affect the N classification.

The intrapelvic and the inguinal nodes are considered regional after scrotal or inguinal surgery.

pNx    Regional lymph nodes cannot be assessed.

pN0    No regional lymph node metastasis.

pN1    Metastasis with a lymph node mass 2 cm or less in greatest dimension and five or fewer positive nodes, none more than 2 cm in greatest dimension.

pN2    Metastasis with a lymph node mass more than 2 cm but not more than 5 cm in greatest dimension; or more than five nodes positive, none more than 5 cm; or evidence of extranodal extension of tumour.

pN3    Metastasis with a lymph node mass more than 5 cm in greatest dimension.
pM  Distant metastasis
pM1  Distant metastasis.
   pM1a  Non-regional lymph node(s) or lung.
   pM1b  Other sites.

(Categories pMx and pM0 have been removed in 7th edition TNM. M0 can only be assigned as a clinical stage, not a pathological stage).

S  Serum tumour markers
SX  Serum marker studies not available or not performed.
S0  Serum marker study levels within normal limits.

<table>
<thead>
<tr>
<th>LDH</th>
<th>hCG (mIU/ml)</th>
<th>AFP (ng/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>S1 &lt;1.5 x N and &lt;5000 and &lt;1000</td>
<td></td>
<td></td>
</tr>
<tr>
<td>S2 1.5–10 x N or 5000–50,000 or 1000–10,000</td>
<td></td>
<td></td>
</tr>
<tr>
<td>S3 &gt;10 x N or &gt;50,000 or &gt;10,000</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

N indicates the upper limit of normal for the LDH assay.

Stage grouping
Stage 0  pTis  N0  M0  S0,SX
Stage I  pT1–4  N0  M0  SX
Stage IA  pT1  N0  M0  S0
Stage IB  pT2  N0  M0  S0
   PT3  N0  M0  S0
   pT4  N0  M0  S0
Stage IS  Any pT/TX  N0  M0  S1–3
Stage II  Any pT/TX  N1–3  M0  SX
Stage IIA  Any pT/TX  N1  M0  S0
   Any pT/TX  N1  M0  S1
Stage IIB  Any pT/TX  N2  M0  S0
   Any pT/TX  N2  M0  S1
Stage IIC  Any pT/TX  N3  M0  S0
   Any pT/TX  N3  M0  S1
Stage III  Any pT/TX  Any N  M1, M1a  SX
<table>
<thead>
<tr>
<th>Stage IIIA</th>
<th>Any pT/TX</th>
<th>Any N</th>
<th>M1, M1a</th>
<th>S0</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Any pT/TX</td>
<td>Any N</td>
<td>M1, M1a</td>
<td>S1</td>
</tr>
<tr>
<td>Stage IIIB</td>
<td>Any pT/TX</td>
<td>N1–3</td>
<td>M0</td>
<td>S2</td>
</tr>
<tr>
<td></td>
<td>Any pT/TX</td>
<td>Any N</td>
<td>M1, M1a</td>
<td>S2</td>
</tr>
<tr>
<td>Stage IIIC</td>
<td>Any pT/TX</td>
<td>N1–3</td>
<td>M0</td>
<td>S3</td>
</tr>
<tr>
<td></td>
<td>Any pT/TX</td>
<td>Any N</td>
<td>M1, M1a</td>
<td>S3</td>
</tr>
<tr>
<td></td>
<td>Any pT/TX</td>
<td>Any N</td>
<td>M1b</td>
<td>Any S</td>
</tr>
</tbody>
</table>
## Appendix B  SNOMED coding of testicular tumours

### Table 1: A comparison of SNOMED 2 or 3 with SNOMED CT codes

<table>
<thead>
<tr>
<th>Topographical codes</th>
<th>SNOMED 2 or 3</th>
<th>SNOMED CT terminology</th>
<th>SNOMED CT code</th>
</tr>
</thead>
<tbody>
<tr>
<td>Right testis</td>
<td>T94010 (SNOMED 3) T78010 (SNOMED 2)</td>
<td>Structure of right testis (body structure)</td>
<td>15598003</td>
</tr>
<tr>
<td>Left testis</td>
<td>T94020 (SNOMED 3) T78020 (SNOMED 2)</td>
<td>Structure of left testis (body structure)</td>
<td>6329009</td>
</tr>
<tr>
<td>Testis, side unknown</td>
<td>T94000 (SNOMED 3) T78000 (SNOMED 2)</td>
<td>Testis structure (body structure)</td>
<td>40689003</td>
</tr>
<tr>
<td>Right epididymis</td>
<td>T95010 (SNOMED 3) T79110 (SNOMED 2)</td>
<td>Structure of right epididymis (body structure)</td>
<td>74475002</td>
</tr>
<tr>
<td>Left epididymis</td>
<td>T95020 (SNOMED 3) T79120 (SNOMED 2)</td>
<td>Structure of left epididymis (body structure)</td>
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</tr>
<tr>
<td>Epididymis, side unknown</td>
<td>T95000 (SNOMED 3) T79100 (SNOMED 2)</td>
<td>Epididymis structure (body structure)</td>
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</tr>
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<td>Spermatic cord</td>
<td>T97000 (SNOMED 3) T79300 (SNOMED 2)</td>
<td>Spermatic cord structure (body structure)</td>
<td>49957000</td>
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### Table 2: A comparison of SNOMED 2 or 3 with SNOMED CT codes

<table>
<thead>
<tr>
<th>Morphological codes</th>
<th>SNOMED 2 or 3</th>
<th>SNOMED CT terminology</th>
<th>SNOMED CT code</th>
</tr>
</thead>
<tbody>
<tr>
<td>Seminoma, classical</td>
<td>M90613</td>
<td>Seminoma, no ICD-O subtype (morphologic abnormality)</td>
<td>36741007</td>
</tr>
<tr>
<td>Spermatocytic seminoma</td>
<td>M90633</td>
<td>Spermatocytic seminoma (morphologic abnormality)</td>
<td>9294008</td>
</tr>
<tr>
<td>Embryonal carcinoma</td>
<td>M90703</td>
<td>Embryonal carcinoma (morphologic abnormality)</td>
<td>28047004</td>
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<tr>
<td>Germ cell tumour, non-seminomatous</td>
<td>M90653</td>
<td>Germ cell tumour, non-seminomatous (morphologic abnormality)</td>
<td>128766005</td>
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<tr>
<td>Teratoma</td>
<td>M90803</td>
<td>Teratoma, malignant, no ICD-O subtype (morphologic abnormality)</td>
<td>19467007</td>
</tr>
<tr>
<td>Choriocarcinoma</td>
<td>M91003</td>
<td>Choriocarcinoma, no ICD-O subtype (morphologic abnormality)</td>
<td>44769000</td>
</tr>
<tr>
<td>Yolk sac tumour</td>
<td>M90713</td>
<td>Endodermal sinus tumour (morphologic abnormality)</td>
<td>74409009</td>
</tr>
<tr>
<td>Mixed embryonal carcinoma and teratoma</td>
<td>M90813</td>
<td>Teratocarcinoma (morphologic abnormality)</td>
<td>67830002</td>
</tr>
<tr>
<td>Tumour Type</td>
<td>Procedure Code</td>
<td>Description</td>
<td>Code</td>
</tr>
<tr>
<td>-------------------------------------</td>
<td>----------------</td>
<td>---------------------------------------------------------------</td>
<td>------------</td>
</tr>
<tr>
<td>Mixed teratoma and seminoma</td>
<td>M90853</td>
<td>Mixed germ cell tumour (morphologic abnormality)</td>
<td>32844007</td>
</tr>
<tr>
<td>Leydig cell tumour</td>
<td>M86501</td>
<td>Leydig cell tumour, no ICD-O subtype (morphologic abnormality)</td>
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<td>Malignant Leydig cell tumour</td>
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<td>Leydig cell tumour, malignant (morphologic abnormality)</td>
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<tr>
<td>Sertoli cell tumour</td>
<td>M86401</td>
<td>Sertoli cell tumour, no ICD-O subtype (morphologic abnormality)</td>
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<td>Malignant Sertoli cell tumour</td>
<td>M86403</td>
<td>Sertoli cell carcinoma (morphologic abnormality)</td>
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<tr>
<td>Sex cord stromal tumour</td>
<td>M85901</td>
<td>Sex cord-stromal tumour, no ICD-O subtype (morphologic abnormality)</td>
<td>71440001</td>
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</table>

**Procedure codes (P)**

These are used in SNOMED 2 and SNOMED 3 to distinguish biopsies, partial resections and radical resections to indicate the nature of the procedure.

Local P codes should be recorded. At present, P codes vary according to the SNOMED system in use in different institutions.
Appendix C  Reporting proforma for testicular cancer (orchidectomy)

Surname…………………….. Forenames.......................... Date of birth.................. Sex…..
Hospital.......................... Hospital no...................... NHS/CHI no...................
Date of receipt.................. Report no.......................... Surgeon..........................

Nature of specimen/procedure and core macroscopic items

Biopsy □ Right □ Radical orchidectomy □ Right □ Left □ Partial orchidectomy □ Left □

Tumour location ..........................
Tumour description ..........................

Macroscopic tunica vaginalis invasion: Yes □ No □ Not assessable □
Cord invasion: Yes □ No □ Not assessable □
Multifocality: Yes □ No □ Not assessable □

Maximum tumour size if assessable: ........ (mm)

Core microscopic items

1. Tumour typing – state percentage of each tumour element present

<table>
<thead>
<tr>
<th>Tumour type/s (one or more)</th>
<th>Germ cell tumour</th>
<th>%</th>
<th>Non-germ cell tumour</th>
</tr>
</thead>
<tbody>
<tr>
<td>Classical seminoma</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Embryonal carcinoma</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yolk sac tumour</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Choriocarcinoma</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Teratoma</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Scar</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Scar</td>
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<td></td>
</tr>
<tr>
<td>Other</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Please specify:.........................</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
2. Tumour parameters

Maximum tumour dimension (if not assessed macroscopically): .................. mm

Lymphovascular invasion (score equivocal foci as negative, i.e. not identified):
Present □  Not identified □  Cannot be assessed □

If lymphovascular invasion present, state which element is showing lymphovascular invasion:
Embryonal carcinoma □  Yolk sac tumour □  Choriocarcinoma □
Teratoma □  Classical seminoma □  Not assessable □

Rete testis stroma invasion:
Yes □  No □  Not assessable □

Hilar soft tissue invasion (pT3)
Yes □  No □  Not assessable □

Direct spermatic cord invasion (pT3)
Yes □  No □  Not assessable □

Tumour at spermatic cord margin (cut end of cord):
Yes □  No □  Not assessable □

Microscopic tunica vaginalis invasion:
Yes □  No □  Not assessable □

IGCNU identified:
Yes □  No □  Not assessable □

Margin status (partial orchidectomy only):
Involved □  Not involved □  Uncertain □  Not applicable □
If not involved, distance to margin ........ mm

Tumour viability (post chemotherapy only):
Viable □  Non- or semi-viable □

pT stage: ...........

SNOMED codes:
T.................. M....................
T.................. M.....................

Signature of pathologist ..................................................  Date ........................................
Appendix D  Reporting proforma for testicular cancer
(retroperitoneal lymph node dissections, other lymph node
excisions or resections of metastatic deposits)

Surname……………………..… Forenames……………………… Date of birth……………. Sex…..
Hospital…………………….. Hospital no…………………….. NHS/CHI no…………………
Date of receipt………………… Report no……………………….. Surgeon…………………

Clinical information required
History of chemotherapy (if known)……..

Nature of specimen/procedure and core macroscopic items
Retroperitoneal lymph node dissection □ Other □ Please specify…………………
Size of specimen (3 dimensions): ........ x ........ x ....... mm
Size of any lymph node masses present: ....... mm

Core microscopic items
1. Tumour typing – state percentage of each viable tumour element present.

<table>
<thead>
<tr>
<th>Tumour type/s (one or more)</th>
<th>Germ cell tumour</th>
<th>%</th>
<th>Non-germ cell tumour</th>
</tr>
</thead>
<tbody>
<tr>
<td>Classical seminoma</td>
<td></td>
<td></td>
<td>Please specify</td>
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<tr>
<td>Embryonal carcinoma</td>
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<td>Choriocarcinoma</td>
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</tr>
<tr>
<td>Semi-viable tumour, non-viable tumour, necrosis or fibrosis only (no viable tumour)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Please specify:.......................</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

2. Tumour parameters
Maximum tumour dimension (if not assessed macroscopically): ............. mm
Number of positive lymph nodes: .......
Total number of lymph nodes: .......
Margin status:
Involved □  Not involved □  Uncertain □  Not applicable □
If not involved, distance to margin .......mm

Tumour viability (post-chemotherapy specimens):
Viable □  Non- or semi-viable □

Extranodal spread of tumour (RPLND or other lymph node excision only):
Yes □  No □  Not assessable □

pT stage: ............

SNOMED codes:
T……………….. M………………..
T……………….. M………………..

Signature of pathologist ...........................................  Date ......................................
### Appendix E  Summary table – Explanation of levels of evidence
(modified from Palmer K et al. BMJ 2008; 337:1832)

<table>
<thead>
<tr>
<th>Level of evidence</th>
<th>Nature of evidence</th>
</tr>
</thead>
</table>
| **Level A**       | At least one high-quality meta-analysis, systematic review of randomised controlled trials or a randomised controlled trial with a very low risk of bias and directly attributable to the target cancer type  
  or  
  A body of evidence demonstrating consistency of results and comprising mainly well-conducted meta-analyses, systematic reviews of randomised controlled trials or randomised controlled trials with a low risk of bias, directly applicable to the target cancer type. |
| **Level B**       | A body of evidence demonstrating consistency of results and comprising mainly high-quality systematic reviews of case-control or cohort studies and high-quality case-control or cohort studies with a very low risk of confounding or bias and a high probability that the relation is causal and which are directly applicable to the target cancer type  
  or  
  Extrapolation evidence from studies described in A. |
| **Level C**       | A body of evidence demonstrating consistency of results and including well-conducted case-control or cohort studies and high quality case-control or cohort studies with a low risk of confounding or bias and a moderate probability that the relation is causal and which are directly applicable to the target cancer type  
  or  
  Extrapolation evidence from studies described in B. |
| **Level D**       | Non-analytic studies such as case reports, case series or expert opinion  
  Or  
  Extrapolation evidence from studies described in C. |
| **Good practice point (GPP)** | Recommended best practice based on the clinical experience of the authors of the writing group |
The cancer datasets of The Royal College of Pathologists comply with the AGREE standards for good quality clinical guidelines (www.agreecollaboration.org). The sections of this dataset that indicate compliance with each of the AGREE standards are indicated in the table.

<table>
<thead>
<tr>
<th>AGREE standard</th>
<th>Section of dataset</th>
</tr>
</thead>
<tbody>
<tr>
<td>SCOPE AND PURPOSE</td>
<td></td>
</tr>
<tr>
<td>1. The overall objective(s) of the guideline is (are) specifically described</td>
<td>Foreword</td>
</tr>
<tr>
<td>2. The clinical question(s) covered by the guidelines is (are) specifically described</td>
<td>Introduction</td>
</tr>
<tr>
<td>3. The patients to whom the guideline is meant to apply are specifically described</td>
<td>Introduction</td>
</tr>
<tr>
<td>STAKEHOLDER INVOLVEMENT</td>
<td></td>
</tr>
<tr>
<td>4. The guideline development group includes individuals from all the relevant professional groups</td>
<td>Foreword</td>
</tr>
<tr>
<td>5. The patients’ views and preferences have been sought</td>
<td>N/A</td>
</tr>
<tr>
<td>6. The target users of the guideline are clearly defined</td>
<td>Introduction</td>
</tr>
<tr>
<td>7. The guideline has been piloted among target users</td>
<td>Introduction</td>
</tr>
<tr>
<td>RIGOUR OF DEVELOPMENT</td>
<td></td>
</tr>
<tr>
<td>8. Systematic methods were used to search for evidence</td>
<td>Foreword</td>
</tr>
<tr>
<td>9. The criteria for selecting the evidence are clearly described</td>
<td>Foreword</td>
</tr>
<tr>
<td>10. The methods used for formulating the recommendations are clearly described</td>
<td>Foreword</td>
</tr>
<tr>
<td>11. The health benefits, side effects and risks have been considered in formulating the recommendations</td>
<td>Foreword and Introduction</td>
</tr>
<tr>
<td>12. There is an explicit link between the recommendations and the supporting evidence</td>
<td>All sections</td>
</tr>
<tr>
<td>13. The guideline has been externally reviewed by experts prior to its publication</td>
<td>Foreword</td>
</tr>
<tr>
<td>14. A procedure for updating the guideline is provided</td>
<td>Foreword</td>
</tr>
<tr>
<td>CLARITY OF PRESENTATION</td>
<td></td>
</tr>
<tr>
<td>15. The recommendations are specific and unambiguous</td>
<td>All sections</td>
</tr>
<tr>
<td>16. The different options for management of the condition are clearly presented</td>
<td>All sections</td>
</tr>
<tr>
<td>17. Key recommendations are easily identifiable</td>
<td>5 and 6</td>
</tr>
<tr>
<td>18. The guideline is supported with tools for application</td>
<td>Appendices</td>
</tr>
<tr>
<td>APPLICABILITY</td>
<td></td>
</tr>
<tr>
<td>19. The potential organisational barriers in applying the recommendations have been discussed</td>
<td>Foreword</td>
</tr>
<tr>
<td>20. The potential cost implications of applying the recommendations have been considered</td>
<td>Foreword</td>
</tr>
<tr>
<td>21. The guideline presents key review criteria for monitoring and/audit purposes</td>
<td>11</td>
</tr>
<tr>
<td>EDITORIAL INDEPENDENCE</td>
<td></td>
</tr>
<tr>
<td>22. The guideline is editorially independent from the funding body</td>
<td>Foreword</td>
</tr>
<tr>
<td>23. Conflicts of interest of guideline development members have been recorded</td>
<td>Foreword</td>
</tr>
</tbody>
</table>

* The Lay Advisory Committee (LAC) of The Royal College of Pathologists advised the Director of Communications that there is no reason to consult directly with patients or the public regarding this dataset because it is technical in nature and intended to guide pathologists in their practice. The authors will refer to the LAC for further advice if necessary.