Imaging Recommendations for Diagnosis, Staging, and Management of Testicular Cancer

Aparna Katdare[1,2] Palak Popat[1,2] Rachel Sequeira[3] Nilesh Sable[1,2] Kunal Gala[1,2] Daksh Chandra[1,2] Archi Agrawal[1,2] Gagan Prakash[1,2] Vedang Murthy[1,2] Santosh Menon[1,2] Amit Joshi[1,2] Ajaykumar Singh[1,2] Suyash Kulkarni[1,2]

[1] Department of Radiodiagnosis, Tata Memorial Centre, Mumbai, Maharashtra, India
[2] Homi Bhabha National Institute, Mumbai, Maharashtra, India
[3] Department of Radiodiagnosis, Mangalore Institute of Oncology, Mangalore, Karnataka, India

Address for correspondence Aparna Katdare, MBBS, DMRD, DNB, Department of Radiodiagnosis, Tata Memorial Centre, Mumbai, Maharashtra 400012, India (e-mail: aparnaringe@yahoo.com).

Ind J Med Paediatr Oncol 2023;44:275–280.

Abstract

The common testicular tumors affect young males in the third and fourth decades and germ cell tumors especially have excellent post-treatment outcomes. Hence, guidelines for clinical, radiological, and tumor marker assessment for diagnosis, response assessment, and surveillance of these tumors have critical impact on the management of these tumors. This article aims to discuss the current recommendations and guidelines regarding the clinical and radiological assessment and treatment pathways of testicular tumors.

Keywords
- guidelines
- imaging
- recommendations
- testicular cancer

Introduction

Testicular malignancies constitute approximately 0.8% of newly diagnosed cases of malignancies in the male population.[1] While the incidence has been on the rise in the recent years, the mortality due to testicular malignancies has been on the decline.[2]

Classification

The World Health Organization (WHO) classification of testicular tumors is given in ►**Table 1**.[3]

Testicular malignancies are classified into germ cell tumors (GCTs) and nongerm cell tumors. GCTs can further be divided into seminomatous and nonseminomatous (NSGCTs). A vast majority of nearly 98% of testicular cancers are GCTs.

Other testicular neoplasms include lymphoma, sarcoma, fibroma, leiomyoma, vascular tumors, and metastases.[4]

Risk Factors and Etiopathogenesis

The etiology of testicular GCTs is still poorly understood, but certain pre-existing medical conditions associated with testicular GCTs include cryptorchidism, radiation, impaired fertility, testicular dysgenesis, and family history or previous history of testicular cancer.[5]

Malignant postpubertal GCTs (type II GCTs) commonly originate from the germ cell neoplasia "in situ" (GCNIS) and are subdivided into seminomas and NSGCTs. The rarer non-related GCNIS tumors comprise pre-pubertal type teratoma and yolk sac tumors (Type I GCT) and spermatocytic tumors (Type III GCT) seen in the elderly.[6]

Epidemiology and Clinical Presentation

The highest incidence of testicular malignancy is in the twenties for NSGCT and in the thirties for seminomas.[7] The less common pre-pubertal type teratomas and yolk sac tumors, and the spermatocytic tumors are diagnosed in prepuberty and elderly age group respectively. About 68% of these malignancies have organ-limited disease while 32% have nodal or distant metastases.[8]

Testicular swelling or pain, scrotal heaviness or lump, dull abdominal, flank or back pain and gynecomastia are common symptoms depending on testicular descent status, hormonal status and nodal or other metastatic disease.

DOI https://doi.org/10.1055/s-0042-1760328.
ISSN 0971-5851.

Thieme Medical and Scientific Publishers Pvt. Ltd., A-12, 2nd Floor, Sector 2, Noida-201301 UP, India

Table 1 The World Health Organization (WHO) 2016 classification of testicular tumors[3]

Germ cell tumors
Germ cell neoplasia in situ (GCNIS)
Derived from GCNIS
Seminoma
Embryonal carcinoma
Yolk sac tumor, postpubertal type
Trophoblastic tumors
Teratoma, postpubertal type
Teratoma with somatic malignant components
Mixed germ cell tumors
Germ cell tumors unrelated to GCNIS
Spermatocytic tumor
Yolk sac tumor, prepubertal type
Mixed germ cell tumor, prepubertal type
Sex cord/stromal tumors
Leydig cell tumor
Malignant Leydig cell tumor
Sertoli cell tumor
Malignant Sertoli cell tumor
Large cell calcifying Sertoli cell tumor
Intratubular large cell hyalinizing Sertoli cell neoplasia
Granulosa cell tumor
Adult type
Juvenile type
Thecoma/fibroma group of tumors
Other sex cord/gonadal stromal tumors
Mixed
Unclassified
Tumors containing both germ cell and sex cord/gonadal stromal—gonadoblastoma
Miscellaneous non-specific stromal tumors
Ovarian epithelial tumors
Tumors of the collecting ducts and rete testis
Adenoma
Carcinoma
Tumors of paratesticular structures
Adenomatoid tumor
Mesothelioma (epithelioid, biphasic)
Epididymal tumors
Cystadenoma of the epididymis
Papillary cystadenoma
Adenocarcinoma of the epididymis
Mesenchymal tumors of the spermatic cord and testicular adnexae

Staging

The American Joint Commission on Cancer staging of testicular malignancy—TNM based on tumor (T), node (N) and metastases (M)—is given in ►**Table 2**[9].

In addition, a unique marker for testicular malignancies is the tumor marker level (α fetoprotein [AFP], β human chorionic gonadotrophin [β-hCG] and lactate dehydrogenase [LDH]), which is included into the International Germ Cell Cancer Collaborative Group (IGCCCG) system of classification of testicular tumors given in ►**Table 3**; this system classifies patients into good, intermediate, and poor risk, taking into account location of tumor and metastases as well as post-orchidectomy tumor markers.[9,10]

Clinical Workup

Clinical History

This should include present symptoms and any history of previous testicular cancer and treatment.

Physical Examination

This includes local site examination and chest, abdominal, and supraclavicular examination.[11]

Hormonal Levels

AFP, β-hCG, and LDH levels are assessed post-orchidectomy. Maintained or rising levels can point to presence of metastases. Normalizing levels post-orchidectomy, although a favorable indicator, do not definitively exclude metastases. Tumor markers are also used for surveillance as indicators of recurrence.[11] Micro-RNAs are promising new biomarkers for diagnosis and monitoring and also for differentiating GCTs from non-GCTs, but not yet included in routine practice and are awaiting standardisation.[12]

Imaging Guidelines

Imaging in testicular malignancies plays an important role in diagnosis, staging, post-treatment disease response assessment, and surveillance.

Diagnosis and Staging

Ultrasound (US)

Ultrasound (US) of testis is done by a high frequency linear transducer (>10 MHz). The objective of US is to localize the scrotal mass (whether testicular or extratesticular), characterize the mass based on morphology, estimate size and volume, look for testicular lesions in known metastatic disease as well as for screening the contralateral testis. US has greater than 90% sensitivity and specificity in diagnosing testicular lesions.[13] Testicular microlithiasis, defined as 5 or more hyperechoic microliths in one US image, is currently not included as an independent risk factor for testicular cancer.[14,15] Contrast-enhanced US is not used routinely, while elastography that reveals increased stiffness in

Table 2 TNM Classification for testicular cancer[28]

pT—Primary tumor
pTX—Primary tumor cannot be assessed
pT0—No evidence of primary tumor
pTis—Intratubular germ cell neoplasia (carcinoma in situ)
pT1—Tumor limited to testis and epididymis without vascular/lymphatic invasion; tumor may invade tunica albuginea but not tunica vaginalis
pT2—Tumor limited to testis and epididymis without vascular/lymphatic invasion, or tumor extending through tunica albuginea with involvement of tunica vaginalis
pT3—Tumor invades spermatic cord with or without vascular/lymphatic invasion
pT4—Tumor invades scrotum with or without vascular/lymphatic invasion
N—Regional Lymph Nodes: Clinical
Nx—Regional lymph nodes cannot be assessed
N0—No regional lymph node metastasis
N1—Metastasis with a lymph node mass 2cm or less in greatest dimension or multiple lymph nodes, none more than 2cm in greatest dimension
N2—Metastasis with a lymph node mass more than 2 cm but not more than 5cm in greatest dimension; or more than 5 nodes positive, none more than 5cm; or evidence of extranodal extension of tumor
N3—Metastasis with a lymph node mass more than 5 cm in greatest dimension
Pn—Regional Lymph Nodes: Pathological
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 5 or fewer positive nodes, none more than 2cm in greatest dimension
pN2—Metastasis with a lymph node mass more than 2cm but not more than 5cm in greatest dimension; or more than 5 nodes positive, none more than 5cm; or evidence of extranodal extension of tumor
pN3—Metastasis with a lymph node mass more than 5cm in greatest dimension
M—Distant metastases
Mx—Distant metastasis cannot be assessed
M0—No distant metastasis
M1—Distant metastasis cannot be assessed
M1a Nonregional lymph node(s) or lung metastasis
M1b Distant metastasis other than nonregional lymph nodes or lung

testicular tumors as compared with benign lesions cannot yet be used as a substitute for histopathological evidence in suspicious lesions.[16,17]

Computed Tomography (CT)

CT is recommended for staging retroperitoneal nodal metastases and for diagnosing pulmonary metastases and mediastinal lymphadenopathy. For retroperitoneal nodal metastases, the left-sided malignancies have propensity for paraaortic nodal involvement and right-sided malignancies for aortocaval nodal involvement due to the drainage of the left-sided and right-sided gonadal veins into the left renal vein and inferior vena cava, respectively.[8] Contrast-enhanced CT study is helpful in better delineation of the nodal size, morphology, and vascular relations. N-staging employs the greatest dimension of the node and the short axis dimension is used for distinguishing between benign and metastatic nodes. While there is no clear consensus for the cutoff value for the short axis diameter, 8 mm or larger can be considered suspicious.[8] In masses up to 2 cm in the retroperitoneum or thorax and negative tumor markers, restaging scan after 6 to 8 weeks is advisable instead of starting treatment immediately.[11] CT brain is a recommendation in patients with NSGCT having pulmonary metastases and poor prognosis IGCCCG risk group (beta hCG values $>$ 5,000 UI/L), or in the presence of clinical symptoms,[18] but magnetic resonance imaging (MRI) can be preferred.

Magnetic Resonance Imaging (MRI)

MRI can help in scenarios where US cannot definitively characterize testicular lesions,[4] but is not universally used. Its use is limited to defining location of scrotal lesions (if intra- or extra- testicular), for planning of testis-sparing surgery, and to characterize intratesticular masses when US is inconclusive. Retroperitoneal nodes can also be assessed by MRI if patient is allergic to iodinated contrast of CT. Brain MRI is particularly useful in aggressive tumors such as choriocarcinomas that

Table 3 Prognostic-based staging system for metastatic germ cell cancer (IGCCCG)[10]

Good prognosis group	
Nonseminoma 5-year PFS 90% 5-year survival 96%	All of the following criteria: • Testis/retroperitoneal primary • No nonpulmonary visceral metastases • AFP < 1,000 ng/mL • β-hCG < 5,000 IU/L (1000 ng/mL) • LDH < 1.5 x ULN
Seminoma 5-year PFS 89% 5-year survival 95%	All of the following criteria: • Any primary site • No nonpulmonary visceral metastases • Normal AFP • Any β-hCG • Any LDH
Intermediate prognosis group	
Nonseminoma 5-year PFS 78% 5-year survival 89%	Any of the following criteria: • Testis/retroperitoneal primary • No nonpulmonary visceral metastases • AFP 1,000–10,000 ng/mL • β-hCG 5,000–50,000 IU/L (1,000 ng/mL) • LDH 1.5–10 x ULN
Seminoma 5-year PFS 79% 5-year survival 88%	All of the following criteria: • Any primary site • Nonpulmonary visceral metastases • Normal AFP • Any β-hCG • Any LDH
Poor prognosis group	
Nonseminoma 5-year PFS 54% 5-year survival 67%	Any of the following criteria: • Mediastinal primary • Nonpulmonary visceral metastases • AFP > 10,000 ng/mL • β-hCG > 50,000 IU/L (10,000 ng/mL) • LDH > 10 x ULN
Seminoma	No patients classified as "poor-prognosis"

Abbreviations: AFP, α fetoprotein; β-hCG, β-human chorionic gonadotrophin; IGCCCG, International Germ Cell Cancer Collaborative Group; LDH, lactate dehydrogenase; PFS, progression-free survival; ULN, upper limit of normal.

have propensity for brain metastases. The National Comprehensive Cancer Network (NCCN) recommends brain MRI in seminoma patients with pulmonary metastasis or β-hCG more than 5,000 IU/L. In NSGCTs, brain MRI is recommended when serum AFP is more than 10,000 ng/mL, β-hCG is more than 5,000 IU/L, and in the presence of visceral or extra-pulmonary metastases or neurological symptoms.[19]

Bone Scan and Fluorine-18 Fluorodeoxyglucose Positron Emission Tomography /CT (18F-FDG-PET/CT)

These are not recommended in initial staging studies.

Response Assessment and Surveillance

Computed Tomography

CT is the modality of choice to evaluate treatment response and diagnose disease recurrence. The standardized Response Evaluation Criteria in Solid Tumors (RECIST 1.1) is used to label response as complete response, partial response, stable disease, and progressive disease. The National Comprehensive Cancer Network (NCCN) guidelines recommend surveillance by CT for 3 to 5 years or beyond after treatment, the frequency of scan depending on tumor histology, stage, treatment, and risk factors.[19]

Magnetic Resonance Imaging

In patients with allergy to iodinated contrast, MRI can be used for restaging instead of CT.

18F-FDG-PET/CT study

PET/CT study is not a part of guidelines for initial staging, but in the restaging scenario, especially in seminomas, 18F-FDG-PET/CT study is of value to differentiate between viable and nonviable residual lesions based on FDG avidity and CT morphology characteristics; indeed, it has shown decrease in overtreatment of seminomas.[20,21] Various studies have shown positive predictive values ranging from 30 to 69%.[22–24] Current recommendations include using 18F-FDG-PET/CT study in post-treatment seminomas with residual mass more than 3 cm. It should be delayed until at least 2 months post last chemotherapy cycle, to prevent false positive findings as a result of inflammation and desmoplastic reaction induced by chemotherapy.[25] 18F-FDG PET/CT in the surveillance setting can be used in certain patients with advanced stage seminoma. 18F-FDG-PET/CT is not recommended in response assessment or surveillance in other testicular tumor subtypes.[19]

Screening

There is no evidence of screening of asymptomatic patients having any utility in detecting testicular carcinoma at a more curable stage.[26]

Management Principles

Orchidectomy, by dividing the spermatic cord at the internal inguinal ring, is the initial diagnostic and partially therapeutic step in patients with testicular cancer. Prosthesis may be offered at the time of surgery or later. Contralateral testicular biopsy is not done routinely but can be considered in patients with high risk for contralateral tumor, such as volume of testis less than 12 mL with or without cryptorchidism.[11] All patients should be offered semen preservation and fertility assessment prior to treatment by estimation of testosterone, follicle-stimulating hormone, and luteinizing hormone levels.[27] Histopathological evaluation of testicular cancer can be supplemented with specific immunohistochemical markers with comment on the presence of lymphovascular infiltration, rete testis involvement, tumor size, and proportion of each histological component in mixed NSGCTs.[11]

The European Association of Urology (EAU) recommends tailoring of treatment according to patient risk profile in testicular tumors post-orchidectomy after discussing all options. Some broad principles of the recommendations are described below.[11]

Local radiotherapy can be considered for GCNIS. Seminomas clinical stage 1 can have subclinical retroperitoneal metastases in up to 15% patients; hence treatment options including surveillance, adjuvant chemotherapy, and adjuvant radiotherapy have to be tailored to each patient. In NSGCT clinical stage 1, options comprise surveillance, adjuvant chemotherapy, or retroperitoneal lymph node dissection (RPLND).

For stage IIA/B seminomas, radiotherapy or alternatively chemotherapy is considered standard of care. In stage II NSGCTs, with elevated tumor marker levels and retroperitoneal nodal disease with elevated tumor levels, primary chemotherapy is the initial treatment of choice, while in retroperitoneal nodal disease without tumor marker elevation, RPLND can be the first-line treatment. For stage IIC/III seminomas as well as NSGCTs, chemotherapy is the initial line of treatment.

Post-treatment residual seminomas are monitored by tumor marker levels and imaging. If residual lesion is less than 3 cm, then observation and follow-up can be considered. If residual lesion is more than 3 cm, a PET/CT is recommended that is usually done 10 to 12 weeks after treatment completion. In patients with residual NSGCTs, if size of residual lesion is more than 1 cm, then it should be resected and if less than 1 cm, then it can be observed on follow-up with imaging and tumor marker levels.

Follow-Up Timelines

The EAU recommends follow-up protocols for different patient subsets as described below.[11]

For seminoma stage 1 on active surveillance or after adjuvant treatment, abdominopelvic CT is recommended at 6 months interval for the initial 2 years, once in the 3rd year and once at 5 years. Tumor markers are assessed at 6 monthly intervals for the initial 3 years and once at 5 years.

For NSGCT stage 1 on active surveillance, abdominopelvic CT is recommended at 6 monthly intervals in the 1st year, annually for the next 2 years, and once at 5 years. Chest radiograph is recommended at 6 monthly intervals in the first 2 years for all patients and once after 3rd and 5th year in case of lymphovascular infiltration. Tumor markers are assessed four times a year in the first 2 years and two times a year for the next 3 years.

For advanced disease after adjuvant treatment or complete remission, thoracoabdominopelvic CT is recommended at 6 monthly intervals in the 1st year, annually in the second and 3rd year and once at 5 years. Chest radiograph is recommended at 6 monthly intervals in the 1st year, annually in the next 2 years and once at 5 years. Tumor markers are assessed four times a year in the first 2 years and twice a year for the next 3 years.

Summary of Recommendations

- US is used for evaluation of scrotal/testicular masses including screening of contralateral testis.
- CT is the primary modality for staging for metastatic disease and for post-treatment restaging and surveillance.
- MRI can be done in patients with iodinated contrast allergy. Brain MRI is used in advanced disease to look for metastases.
- PET/CT study is not recommended for initial staging, but can be useful in restaging of seminomas to distinguish between viable and nonviable residual lesions.
- Tumor markers are useful in conjunction with imaging for initial risk stratification and in follow-up and surveillance.

Conclusion

Management of testicular malignancies needs multidisciplinary approach by radiologists, pathologists, and treating physicians. Imaging along with tumor marker levels is crucial in staging, risk stratification, assessing treatment response, and for surveillance. Decision-making regarding treatment algorithms and surgical planning is aided by imaging. Since these are potentially curable malignancies in young males, all efforts must be invested by the treating physician team for optimum treatment planning in these patients.

Conflict of Interest
None declared.

References

1 [World Cancer Research Fund. Worldwide Cancer Data: Global cancer statistics for the most common cancers. Accessed December 9, 2022, at: https://www.wcrf.org/dietandcancer/cancer-trends/worldwide-cancer-data].
2 Znaor A, Lortet-Tieulent J, Jemal A, Bray F. International variations and trends in testicular cancer incidence and mortality. Eur Urol 2014;65(06):1095–1106
3 Williamson SR, Delahunt B, Magi-Galluzzi C, et al; Members of the ISUP Testicular Tumour Panel. The World Health Organization 2016 classification of testicular germ cell tumours: a review and update from the International Society of Urological Pathology Testis Consultation Panel. Histopathology 2017;70(03):335–346
4 Mittal PK, Abdalla AS, Chatterjee A, et al. Spectrum of extratesticular and testicular pathologic conditions at scrotal MR imaging. Radiographics 2018;38(03):806–830
5 Makovník M, Rejleková K, Uhrin I, Mego M, Chovanec M. Intricacies of radiographic assessment in testicular germ cell tumors. Front Oncol 2021;10:587523 https://www.frontiersin.org/article/10.3389/fonc.2020.587523
6 Looijenga LHJ, Van der Kwast TH, Grignon D, et al. Report From the International Society of Urological Pathology (ISUP) Consultation Conference on Molecular Pathology of Urogenital Cancers: IV: current and future utilization of molecular-genetic tests for testicular germ cell tumors. Am J Surg Pathol 2020;44(07):e66–e79
7 Oosterhuis JW, Looijenga LHJ. Testicular germ-cell tumours in a broader perspective. Nat Rev Cancer 2005;5(03):210–222
8 Hale GR, Teplitsky S, Truong H, Gold SA, Bloom JB, Agarwal PK. Lymph node imaging in testicular cancer. Transl Androl Urol 2018;7(05):864–874
9 Magers MJ, Idrees MT. Updates in staging and reporting of testicular cancer. Surg Pathol Clin 2018;11(04):813–824

10 International Germ Cell Cancer Collaborative Group. International Germ Cell Consensus Classification: a prognostic factor-based staging system for metastatic germ cell cancers. J Clin Oncol 1997; 15(02):594–603
11 Laguna M, et al. EAU guidelines on testicular cancer 2022. Accessed December 9, 2022, at: http://www.uroweb.org/guideline/testicularcancer/
12 Lobo J, Leão R, Gillis AJM, et al. Utility of Serum miR-371a-3p in predicting relapse on surveillance in patients with clinical stage I testicular germ cell cancer. Eur Urol Oncol 2021;4(03):483–491
13 Wilson SR, Greenbaum LD, Goldberg BB. Contrast-enhanced ultrasound: what is the evidence and what are the obstacles? AJR Am J Roentgenol 2009;193(01):55–60
14 Coursey Moreno C, Small WC, Camacho JC, et al. Testicular tumors: what radiologists need to know–differential diagnosis, staging, and management. Radiographics 2015;35(02):400–415
15 Winter TC, Kim B, Lowrance WT, Middleton WD. Testicular microlithiasis: what should you recommend? AJR Am J Roentgenol 2016;206(06):1164–1169
16 Lock G, Schmidt C, Helmich F, Stolle E, Dieckmann KP. Early experience with contrast-enhanced ultrasound in the diagnosis of testicular masses: a feasibility study. Urology 2011;77(05):1049–1053
17 Aigner F, De Zordo T, Pallwein-Prettner L, et al. Real-time sonoelastography for the evaluation of testicular lesions. Radiology 2012;263(02):584–589
18 Feldman DR, Lorch A, Kramar A, et al. Brain metastases in patients with germ cell tumors: Prognostic factors and treatment options - an analysis from the Global Germ Cell Cancer Group. J Clin Oncol 2016;34(04):345–351
19 National Comprehensive Cancer Network NCCN Clinical Practice Guidelines in Oncology. Testicular Cancer. Version 1.2019. October 22, 2018. Accessed December 9, 2022, at: https://www.nccn.org/professionals/physician_gls/pdf/testicular.pdf
20 Necchi A, Nicolai N, Alessi A, et al. Interim 18F-Fluorodeoxyglucose Positron Emission Tomography for Early Metabolic Assessment of Response to Cisplatin, Etoposide, and Bleomycin Chemotherapy for Metastatic Seminoma: Clinical Value and Future Directions. In: *Clinical Genitourinary Cancer*. Vol 14.; 2016 Doi: 10.1016/j.clgc.2015.08.010
21 Honecker F, Aparicio J, Berney D, et al. ESMO consensus conference on testicular germ cell cancer: diagnosis, treatment and follow-up. In: *Annals of Oncology*. Vol 29.; 2018 Doi: 10.1093/annonc/mdy217
22 Bachner M, Loriot Y, Gross-Goupil M, et al. 2-^{18}fluoro-deoxy-D-glucose positron emission tomography (FDG-PET) for postchemotherapy seminoma residual lesions: a retrospective validation of the SEMPET trial. Ann Oncol 2012;23(01):59–64
23 Cathomas R, Klingbiel D, Bernard B, et al. Questioning the value of fluorodeoxyglucose positron emission tomography for residual lesions after chemotherapy for metastatic seminoma: results of an International Global Germ Cell Cancer Group Registry. J Clin Oncol 2018;36(34):JCO1800210. Doi: 10.1200/JCO.18.00210
24 Murthy V, Karmakar S, Carlton J, et al. Radiotherapy for post-chemotherapy residual mass in advanced seminoma: a fluorodeoxyglucose positron emission tomography-computed tomography-based risk-adapted approach. Clin Oncol (R Coll Radiol) 2021;33(07):e315–e321
25 Oechsle K, Hartmann M, Brenner W, et al; German Multicenter Positron Emission Tomography Study Group. [18F]Fluorodeoxyglucose positron emission tomography in nonseminomatous germ cell tumors after chemotherapy: the German multicenter positron emission tomography study group. J Clin Oncol 2008;26 (36):5930–5935
26 Ilic D, Misso ML. Screening for testicular cancer. Cochrane Database Syst Rev 2011;(02):CD007853
27 Gilbert K, Nangia AK, Dupree JM, Smith JF, Mehta A. Fertility preservation for men with testicular cancer: is sperm cryopreservation cost effective in the era of assisted reproductive technology? Urol Oncol 2018;36(03):92.e1–92.e9
28 Brierley JE, et al. The TNM Classification of Malignant Tumours 8th edition. 2016. Accessed December 9, 2022, at: https://www.uicc.org/resources/tnm-classification-malignant-tumours-8th-edition