Diagnosis and Treatment of Early-Stage Testicular Cancer (2023)

About the Guideline

- The guideline panel, amendment panel, staff, and consultants consisted of 19 physicians and other professionals.
- The panel provided 43 recommendations regarding the diagnosis and treatment of early-stage testicular cancer. The literature search was conducted from January 1980 through August 2018, and again through March 2023, using PubMed, Embase, and the Cochrane Central Register of Controlled Trials (CENTRAL).
- This guideline provides recommendations regarding the diagnosis, staging, treatment selection, and posttreatment surveillance of patients with clinical stages I, IIA, and IIB seminoma and nonseminomatous germ cell tumors (NSGCT).

Key Clinical Considerations

Become familiar with the recommendations and best-practice statements provided in this guideline, especially if you work in an acute care setting.

Introduction

- Testicular cancer is the most common solid malignancy in young males (defined as ages 20 to 40 years old).
- Testicular cancer is a relatively rare cancer, with standard therapy providing high survival rates.
- Risk factors for testicular cancer include the following:
    - Germ cell neoplasia in situ (GCNIS)
    - History of undescended testis (UDT) or cryptorchidism
    - Family history
    - Personal history of testicular cancer
- The tumor markers used to determine diagnosis, prognosis, clinical staging, management, and response to therapy as well as for posttreatment surveillance include the following:
    - Alpha-fetoprotein (AFP)
        - Elevated in 10% to 40% of low-stage (clinical stages I, IIA, IIB) NSGCT
    - Human chorionic gonadotropin (hCG)
        - Elevated in 10% to 30% of low-stage NSGCT and in 10% to 15% of seminomas
    - Lactate dehydrogenase (LDH)
        - Elevated in approximately 20% of low-stage germ cell tumor (GCT)
        - Least relevant and clinically applicable
- Clinical staging dictates prognosis and initial management and is determined by the staging system developed by the American Joint Committee on Cancer (AJCC) and the Union Internationale Contre le Cancer (UICC).
    - Disease clinically confined to the testis is considered clinical stage I.
    - Disease with regional (retroperitoneal) lymph node metastasis is considered clinical stage II.
    - Disease with nonregional lymph node, lung, and/or visceral metastasis is considered clinical stage III.

Initial Management

- Testicular cancer most commonly presents as a painless, enlarging mass. If a solid mass is found by physical exam or by imaging, the mass should be managed as malignant until a neoplasm has been ruled out.
- For patients with a suspicious, solid testicular mass, serum tumor markers should be drawn and evaluated prior to any treatment.
- Patients should be counseled regarding the risks of hypogonadism and infertility and offered sperm banking prior to definitive management.
    - Prior to orchiectomy, consider offering sperm banking to patients without a normal contralateral testis or with known subfertility.
- Perform ultrasonography (of the scrotum) for patients with a unilateral or bilateral suspicious scrotal mass.
- Testicular microlithiasis does not present an increased risk of malignancy in the absence of risk factors and a solid mass.
    - Patients with testicular microlithiasis and risk factors should be educated regarding the potential increased risk of GCT, the importance of performing periodic self-examinations, and following up with their provider.
- Repeat imaging in 6 to 8 weeks for patients with normal serum tumor markers and indeterminate physical exam findings or testicular ultrasound.
- For the initial evaluation and diagnosis of suspicious testicular lesions, magnetic resonance imaging (MRI) is not recommended.
    - For patients with lesions suspicious for benign etiology, MRI may be considered as an adjunct to ultrasonography (scrotum).
- For patients with a suspicious testicular lesion and a normal contralateral testis, perform a radical inguinal orchiectomy; testis-sparing surgery (TSS) is not recommended, and trans scrotal orchiectomy is not suggested.
- Prior to orchiectomy, testicular prosthesis should be discussed.
- Counsel patients who have undergone scrotal orchiectomy regarding the increased risk of local recurrence. Adjunctive therapy with excision of scrotal scar or radiotherapy may be considered in rare cases.
    - If malignancy is suspected, transscrotal orchiectomy and transscrotal biopsy are not recommended, as these procedures are associated with significantly higher rates of local recurrence.

Testis-Sparing Surgery (TSS)

- For select patients with masses less than 2 cm and who wish to preserve gonadal function, TSS through an inguinal incision may be offered as an alternative to radical inguinal orchiectomy if they meet one of the following criteria:
    - Ambiguous ultrasound and physical exam findings, and negative tumor markers, or
    - Congenital, acquired or functionally solitary testis, or
    - Bilateral synchronous tumors.
- Counsel patients considering TSS regarding the following:
    - Higher risk of local recurrence
    - Necessity of monitoring with physical examination and ultrasound
    - Role of adjuvant radiotherapy to the testicle to reduce local recurrence
    - Impact of radiotherapy on sperm and testosterone production

    - Risk of testicular atrophy and the need for testosterone replacement therapy and/or subfertility or infertility
- Multiple biopsies of the ipsilateral testicle, in addition to the suspicious mass, should be obtained and evaluated when TSS is performed.
- TSS may be considered for the following patients:
    - Those with a high likelihood of a concealed, benign testicular tumor
    - Patients with an anatomically or functionally single testicle who wish to preserve hormonal function and fertility
    - Those with congenital or acquired single testicle, or with bilateral synchronous malignancy who wish to preserve hormonal function and fertility

GCNIS Counseling and Management

- Patients with a history of GCT or GCNIS should be informed of the rare lifetime risk (2%) of developing a second primary tumor in the contralateral testis.
    - The following increase the risk of a contralateral primary tumor:
        - Testicular atrophy
        - Cryptorchidism
        - Younger age at initial presentation
    - Surveillance and early detection of a contralateral primary tumor can be achieved with routine testicular self-examinations.
- Fifty percent of patients with GCNIS on biopsy will develop testicular cancer over the subsequent five years.
- Management options include the following:
    - Surveillance and expectant management
    - Ipsilateral radiation
        - Radiation is associated with higher rates of hypogonadism compared with surveillance; however, it reduces the rates of a second GCT or persistent GCNIS.
    - Orchiectomy
        - Radical orchiectomy is considered the most definitive treatment and eliminates the risk of GCNIS; however, it is associated with higher rates of infertility and hypogonadism.
    - Chemotherapy is not recommended due to lack of efficacy.
- Discussion should include sperm banking and treatment of hypogonadism, as appropriate.
- For patients who desire future paternity without the need for assisted reproductive techniques, expectant management with deferred radiation or orchiectomy may be considered.
    - Close monitoring and adherence to follow-up is vital.

Staging

- For staging and risk stratification, nadir serum tumor markers should be repeated at routine intervals after an orchiectomy.
    - Using pre-orchiectomy markers for staging and risk stratification may lead to under- or overtreatment.
- For postorchiectomy patients with an elevated alpha-fetoprotein (AFP) level or human chorionic gonadotropin (hCG) levels, monitor levels before treatment only if marker nadir levels will influence treatment.

- The International Germ Cell Cancer Collaborative Group (IGCCCG) Consensus Classification is used for risk stratification and considers the following criteria for prognosis (classified as good, intermediate, and poor):
    - Histology (seminoma versus nonseminoma)
    - Presence or absence of nonpulmonary visceral metastasis
    - Serum tumor marker levels following orchiectomy (and prior to initiation of chemotherapy)
    - Staging imaging studies
- For patients with metastatic GCT requiring chemotherapy, the chemotherapy regimen and number of cycles is based on the IGCCCG risk stratification.
- Before decisions in management are made, confirm any trend in rising marker levels for postorchiectomy patients with borderline elevated AFP and hCG levels, as rising levels are not always indicative of GCT.

Imaging

- Obtain chest imaging, and cross-sectional imaging of the abdomen and pelvis with IV contrast (or MRI if computerized tomography scanning [CT] is contraindicated), for patients with newly diagnosed GCT.
    - At diagnosis, imaging of the retroperitoneum and pelvis is necessary for staging and treatment selection.
- For patients with elevated and rising postorchiectomy markers (hCG and AFP) or evidence of metastases present on abdominal/pelvic imaging, chest x-ray, or physical exam, a chest CT should be performed.
- For patients with clinical stage I seminoma, chest x-ray is preferred over CT scan.
- For patients with NSGCT, chest CT may be preferred over chest x-ray, and should be prioritized for patients whose treatment plan includes adjuvant therapy to ensure that no evidence of metastasis is present prior to proceeding with therapy.
- Positron emission tomography (PET) scan is not recommended for staging in patients newly diagnosed with GCT.
- A TNM-s category should be assigned to patients to guide treatment decisions.

Management

- Management decisions should be made in a timely manner due to the rapid doubling time of GCT and NSGCT. There is a risk of disease progression if there is significant delay between staging studies and initiation of treatment.
    - Decisions should be based serum tumor markers (hCG and AFP) assessed within the preceding 10 days, and imaging performed within the preceding 4 weeks.
- A multidisciplinary team, including urology, medical oncology, radiation oncology, pathology, and radiology, should be involved in making management decisions.
- To determine the extent of disease, consider repeat imaging in 6 to 8 weeks prior to making treatment decisions for patients with normal serum tumor markers (hCG and AFP) and metastasis noted on imaging.

Seminoma Management

- For patients with stage I seminoma, surveillance is recommended after orchiectomy over adjuvant radiotherapy and chemotherapy.

- For patients with stage IIA or IIB seminoma with a lymph node 3 cm or less, radiation therapy (RT) or multiagent chemotherapy is recommended.
- For patients with stage IIA or IIB seminoma with a lymph node 3 cm or less who would like to avoid the long-term effects and toxicities associated with RT or chemotherapy, retroperitoneal lymph node dissection (RPLND) may be considered.
- For patients with IIB seminoma with a lymph node more than 3 cm, chemotherapy is recommended.

Nonseminoma Management

- For patients with NSGCT with elevated and rising postorchiectomy serum hCG and AFP, risk-appropriate chemotherapy is recommended.
- For patients with stage IA NSGCT, surveillance is recommended. For patients who decline surveillance or who are at high risk of nonadherence, RPLND or one cycle of chemotherapy may be an effective alternative.
- For patients with stage IB NSGCT, treatment options include the following:
    - Surveillance, or
    - RPLND, or
    - Two cycles of chemotherapy.
- RPLND should be performed for patients with stage I NSGCT with any secondary somatic malignancy noted in the primary tumor during orchiectomy.
- For patients with stage IIA NSGCT and normal postorchiectomy serum hCG and AFP, treatment with RPLND or chemotherapy is recommended.
- Risk-appropriate, multiagent chemotherapy is recommended for patients with clinical stage IIB NSGCT and normal postorchiectomy hCG and AFP.
    - RPLND may be offered as an alternative to chemotherapy to select patients.
- Consider referral to an experienced surgeon for patients eligible for RPLND.
- Perform primary RPLND with curative intent for all patients.
    - Case-specific lymph node dissection and nerve-sparing techniques should be applied to both open and minimally invasive surgical approaches.
- For patients with NSGCT and pathological stage II disease that is not pure teratoma, surveillance or adjuvant chemotherapy is recommended after primary RPLND.
    - Surveillance is preferred for patients with pN1 and/or pN1—3 teratoma.
    - Multiagent chemotherapy is preferred for patients with pN2—3 at the time of RPLND.

Surveillance for Stage I Testicular Cancer

- Surveillance should include a history and physical examination and cross-sectional imaging of the abdomen, with or without the pelvis, performed at the following intervals:
    - Every 6 months for the first 2 years, followed by every 6 to 12 months for the next 3 to 5 years.
    - Routine chest imaging and serum tumor marker levels should be performed as clinically indicated.
- Surveillance postorchiectomy should include a physical examination and serum tumor markers (AFP, hCG, with or without LDH) every 2 to 3 months for 1 year, every 2 to 4 months in year 2, every 4 to 6 months in year 3, and every 6 to 12 months for years 4 and 5.
    - Chest x-ray and imaging of the abdomen with or without the pelvis should be performed every 3 to 6 months in year 1, every 4 to 12 months in year 2, and annually in years 3, 4, and 5.

Survivorship

- Patients should be referred to a survivorship clinic to assist in managing long-term risks and effects of treatment.

Reference

Stephenson, A., Eggener, S. E., Bass, E. B., Chelnick, D. M., Daneshmand, S., Feldman, D., Gilligan, T., Karam, J. A., Leibovich, B., Liauw, S. L., Masterson, T. A., Meeks, J. J., Pierorazio, P. M., Sharma, R., & Sheinfeld, J. (2019). Diagnosis and Treatment of Early Stage Testicular Cancer: AUA Guideline. *The Journal of urology*, *202*(2), 272–281. https://doi.org/10.1097/JU.0000000000000318