The optimal management of clinical stage I testicular germ cell tumors remains controversial despite a cure rate of 99%. Alternatives for stage I nonseminomas include close surveillance, retroperitoneal lymph node dissection, and chemotherapy. For pure seminomas, the options are surveillance, chemotherapy, and radiation. Understanding the pros and cons of each approach may help in choosing a management plan.

Introduction

Testicular cancer is the most common cancer in young men aged 20 to 35 but is one of the most curable solid malignancies, with a 5-year survival rate greater than 95%. In 2008, an estimated 8090 men in the United States were diagnosed with testicular cancer and 380 died of this disease [1]. Approximately 60% of testicular germ cell tumors (GCTs) are pure seminomas, and the other 40% are non-seminomatous GCTs (NSGCTs), most of which are mixed GCTs. Seventy percent of these malignancies are diagnosed in the early stages, and most are clinical stage I.

Following radical orchiectomy, the available treatment options for stage I testis cancer are surveillance, adjuvant chemotherapy, radiation, and retroperitoneal lymph node dissection (RPLND), alone or in combination. However, the question of which treatment modality is best remains controversial. In this review, we discuss the various management options for stage I seminomas and NSGCTs after radical orchiectomy.

Clinical Stage I Staging Criteria

Clinical stage I disease refers to tumor involvement limited to the testis, epididymis, or spermatic cord, with no nodal or metastatic involvement on radiographic imaging studies. It is worth noting that although patients with persistently elevated serum levels of α-fetoprotein (AFP), human chorionic gonadotropin, or lactate dehydrogenase are classified as stage I, they are treated clinically as stage III. Clinical stage II disease is limited to the retroperitoneal lymph nodes and is divided into stages IIA (nodes < 2 cm in maximal diameter), IIB (nodes between 2 and 5 cm in diameter), and IIC (nodes > 5 cm in diameter). When staging testis cancer, it is important to evaluate the retroperitoneum carefully, because even small nodes in the primary landing zones for testis cancer can signify stage II disease [2]. Fifteen percent to 30% of clinical stage I patients will be upstaged to pathologic stage II after RPLND.

Imaging Studies in Early-Stage Germ Cell Tumors

The primary imaging modality used to determine lymph node involvement is the CT scan. Over- and understaging remain substantial problems, and the optimal size criteria for labeling retroperitoneal lymph nodes enlarged in men with testicular GCTs are not well defined. Even in recent series, there is a 25% to 30% rate of clinical understaging in patients whose scans are read as normal and a 20% to 40% rate of overstaging in patients whose scans are read as showing enlarged nodes [3]. In common practice, lymph nodes with a short-axis diameter of more than 10 mm are considered abnormal, but this cutoff results in a low sensitivity of about 60%. Therefore, some have advocated using a smaller size cutoff for lymph nodes in the primary landing zone to reduce the false-negative rate [2].

The fluorodeoxyglucose positron emission tomography (PET) scan currently has no role in the management of early-stage testis cancer, but it is sometimes used to evaluate residual masses following chemotherapy in patients with metastatic pure seminoma [4–6]. PET has been investigated as a staging tool for men with clinical stage I disease by CT scan criteria but was not found to improve staging accuracy. A recent multinational trial enrolling men with clinical stage I NSGCT reported that 33 of 87 PET-negative patients relapsed on surveillance at a median follow-up of only 12 months [6]. The 1-year relapse-free survival rate was only 63%.
**Table 1. Options for nonseminomatous germ cell tumors**

<table>
<thead>
<tr>
<th>Option</th>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Surveillance</td>
<td>Avoids treatment that is unnecessary for 70% of patients. Most patients thus avoid the complications and side effects of RPLND and chemotherapy.</td>
<td>Patients who relapse typically require a full course of chemotherapy for metastatic testis cancer: 3 cycles of BEP or 4 cycles of EP. Higher risk of relapse than with RPLND or chemotherapy and thus potential for increased patient anxiety. Requires patient compliance and long-term access to medical care.</td>
</tr>
<tr>
<td>RPLND</td>
<td>Reduces the risk of needing chemotherapy&lt;br&gt;Removes teratomatous GCTs, which may be resistant to chemotherapy&lt;br&gt;Reduces the risk of late relapse</td>
<td>Overtreatment for the 70% of patients cured with orchiectomy alone&lt;br&gt;About 20% of patients will still get chemotherapy—as 2 cycles of adjuvant chemotherapy for pathologic stage II disease or a full course for relapse&lt;br&gt;Large surgical scar&lt;br&gt;Risk of loss of ejaculation&lt;br&gt;Major operation&lt;br&gt;Requires highly experienced surgeon.</td>
</tr>
<tr>
<td>1 or 2 cycles of BEP chemotherapy</td>
<td>Reduces risk of relapse to &lt; 3%</td>
<td>Overtreatment for the 70% of patients cured by orchiectomy alone&lt;br&gt;Chemotherapy side effects, some of which may be chronic&lt;br&gt;Potential increased risk of cardiovascular disease and second malignancies due to exposure to chemotherapy&lt;br&gt;Theoretic risk of late relapse from chemoresistant teratomatous GCT.</td>
</tr>
</tbody>
</table>

BEP—bleomycin, etoposide, and cisplatin; EP—etoposide and cisplatin; GCT—germ cell tumor; RPLND—retroperitoneal lymph node dissection.

**Treatment Options for Clinical Stage I NSGCT**

For patients with clinical stage I NSGCT who have normal postorchiectomy serum tumor marker levels, the treatment options are surveillance, RPLND, and primary chemotherapy (Table 1). Each of these approaches is associated with a cure rate of close to 100%, and there is no general consensus on what constitutes best practice [7•]. The choice of treatment therefore is influenced by several factors, including the risk of relapse, the toxicities involved in each approach, the patient’s ability and commitment to comply with a surveillance schedule, access to a urologist who regularly performs RPLNDs, and the patient’s and treating physician’s preferences.

**Risk factors for relapse in stage I NSGCT**

Given that 25% to 30% of clinical stage I NSGCT patients harbor occult metastatic disease, there has been great interest in identifying prognostic factors that would accurately predict which patients would benefit from additional treatment and which could be surveilled with low risk of relapse. Unfortunately, there are no prospectively validated highly accurate prognostic models at this time. The two most widely documented risk factors for relapse following orchiectomy are lymphovascular invasion and a predominance of embryonal carcinoma [8–11]. Approximately 48% of clinical stage I disease relapses when vascular invasion is present, compared with 15% to 20% in its absence. Researchers at Indiana University reported that among men undergoing RPLND who were found to have pathologic stage I disease, the rate of relapse in patients with embryonal carcinoma–predominant disease was 21.2%, compared with 3% in other patients [8]. A retrospective analysis of data from men undergoing RPLND for clinical stage I NSGCT within the US armed services medical system reported metastatic disease in over 75% of clinical stage I patients who had nearly pure embryonal carcinoma or a predominance of embryonal carcinoma plus the presence of lymphovascular invasion [12]. The risk of metastatic disease in patients without these risk factors was less than 15%. Memorial Sloan-Kettering’s experience with RPLND in men with clinical stage I pure embryonal carcinoma revealed that 73% had lymph node metastases and 54% received subsequent chemotherapy [13]. Although there are no studies demonstrating that the use of these risk factors results in superior outcomes, estimates of the risk of relapse may influence patient and physician comfort with different treatment options.

**Role of RPLND in clinical stage I NSGCT**

RPLND offers two benefits: it allows more accurate staging and reduces the risk that chemotherapy will be administered. RPLND also offers the theoretic benefit...