Role of Postchemotherapy Retroperitoneal Lymph Node Dissection in Advanced Germ Cell Tumors

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• Testicular neoplasms • Neoplasms • Germ cell • Embryonal
• Chemotherapy • Retroperitoneum • Lymph node excision
• Neoplasm staging

Testis cancer is the most common malignancy afflicting men between the ages of 15 and 34 years, with 8400 men expected to be diagnosed in the United States in 2010.[1] Most cases (>95%) are germ cell tumors (GCTs), which are broadly divided into seminoma and nonseminoma GCT (NSGCT). Advanced GCT is an example of the importance of multidisciplinary management in the successful treatment of patients. Before the development of cisplatin-based chemotherapy, long-term survival was reported in less than 10% of patients.[2] Long-term cure is now anticipated in 80% to 90%.[3] A recent meta-analysis of 10 trials enrolling a total of 1775 patients with advanced NSGCT reported improved 5-year survival rates for patients with good-risk (94% vs 89%), intermediate-risk (83% vs 75%), and poor-risk disease (71% vs 41%) compared with the original pooled analysis conducted by the International Germ Cell Cancer Collaborative Group (IGCCCG).[3,4] This improved prognosis for patients with advanced GCT is likely caused by better risk stratification and

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risk-appropriate chemotherapy, stage migration, and improved integration of chemotherapy and postchemotherapy surgery (PCS) for resection of residual masses.

For treatment purposes, the distinction between seminoma and NSGCT holds great importance, particularly in the management of residual masses. Compared with NSGCT, seminoma is exquisitely sensitive to cisplatin-based chemotherapy. Thus, residual masses after first-line chemotherapy for seminoma are more likely to show necrosis and less likely to harbor viable GCT elements compared with NSGCT. The risk of teratoma at metastatic sites has a substantial effect on treatment algorithms for NSGCT and necessitates the frequent use of PCS in patients with advanced NSGCT. As discussed later, teratoma is not sensitive to chemotherapy and the outcome of patients with metastatic teratoma is related to the completeness of surgical resection. Although histologically benign, teratoma has unpredictable biology, with a capacity to grow rapidly, undergo malignant transformation, or result in late relapse. The risk of teratoma at metastatic sites is generally not a consideration for advanced seminoma, which has important implications for the management of residual masses after chemotherapy.

Because of the high cure rates anticipated for patients with advanced GCT, numerous clinical trials have been conducted in an attempt to minimize treatment and avoid any unnecessary therapies in an effort to reduce short-term, and particularly long-term, toxicity. One such approach has been to limit the number of patients who receive 2 interventions (double therapy): either surgery or chemotherapy and not both. However, because NSGCTs are usually mixed tumors and teratoma often exists at metastatic sites with other GCT elements, cure often requires chemotherapy to eradicate the chemosensitive components and surgery to remove teratomatous components. It is widely accepted that the successful integration of systemic therapy and PCS is a major contributing factor to the improved cure rates for metastatic GCT seen in the past several decades.

Advances in surgical technique and understanding of retroperitoneal anatomy have reduced the morbidity of RPLND (eg, retrograde ejaculation) while enhancing oncological efficacy. However, postchemotherapy retroperitoneal lymph node dissection (PC-RPLND) can be a challenging undertaking that has historically been associated with higher rates of complications compared with primary RPLND.[5–7] As such, appropriate patient selection and proper surgical technique are critical to optimizing cancer and quality-of-life outcomes following surgery.

The indications and outcomes of PC-RPLND are discussed to determine its role in the contemporary management of advanced GCT. This article focuses primarily on PC-RPLND in the setting of NSGCT, but the limited indications for PCS in advanced seminoma are also discussed.

NSGCT: RATIONALE FOR PC-RPLND

The role of PC-RPLND for residual masses in advanced NSGCT is well established and its rationale is based on several factors. Multiple large series of patients undergoing PC-RPLND for residual masses after first-line chemotherapy have consistently reported evidence of persistent GCT elements in the resected specimens in 50% or more of patients. On average, histopathologic evaluation of resected specimens shows necrosis, teratoma, and viable malignancy (with or without teratoma) in 40%, 45%, and 15% of cases respectively (**Table 1**).[8–20]

The therapeutic benefit of PC-RPLND in cases in which residual masses harbor viable malignancy or teratoma is well documented. Complete resection of viable malignancy (with or without adjuvant chemotherapy) is associated with 5-year survival