Current Role of Retroperitoneal Lymph Node Dissection in Testicular Cancer

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Carcinoma of the testis is the most common malignancy in males 15 to 35 years of age. Testicular cancer has become one of the most curable solid neoplasms and, as such, serves as a paradigm for the multimodality treatment of malignancies. The cure rate for patients with clinical stage I disease is nearly 100%, and patients with advanced disease now achieve complete remission rates of over 90%. The markedly improved outlook for patients with this cancer over the past 15 years has led to a reassessment of management options, especially in patients with clinical stage I disease. The realization that platinum-based chemotherapy could cure most patients with an advanced nonseminomatous germ cell tumor (NSGCT), especially those with minimal disease, led to the introduction of various strategies to decrease the morbidity associated with surgical management. These strategies include surveillance protocols, chemotherapy for clinical stage II disease, and observation protocols for a subset of patients with advanced disease who have had a partial response to chemotherapy. Retroperitoneal lymph node dissection (RPLND) has an important place in the management of both low- and high-stage testicular cancer. It offers the patient two basic benefits: accurate staging and the possibility of a surgical cure, even in the presence of metastatic disease. [ONCOLOGY 11(5):717-729, 1997]

ABSTRACT: Carcinoma of the testis is the most common malignancy in males 15 to 35 years of age. Testicular cancer has become one of the most curable solid neoplasms and, as such, serves as a paradigm for the multimodality treatment of malignancies. The cure rate for patients with clinical stage I disease is nearly 100%, and patients with advanced disease now achieve complete remission rates of over 90%. The markedly improved outlook for patients with this cancer over the past 15 years has led to a reassessment of management options, especially in patients with clinical stage I disease. The realization that platinum-based chemotherapy could cure most patients with an advanced nonseminomatous germ cell tumor (NSGCT), especially those with minimal disease, led to the introduction of various strategies to decrease the morbidity associated with surgical management. These strategies include surveillance protocols, chemotherapy for clinical stage II disease, and observation protocols for a subset of patients with advanced disease who have had a partial response to chemotherapy. Retroperitoneal lymph node dissection (RPLND) has an important place in the management of both low- and high-stage testicular cancer. It offers the patient two basic benefits: accurate staging and the possibility of a surgical cure, even in the presence of metastatic disease. [ONCOLOGY 11(5):717-729, 1997]

Introduction

Despite the fact that carcinoma of the testis accounts for only 1% of all malignancies in males, it is the most common solid malignancy affecting males between the ages of 15 and 35 years. As such, testicular cancer raises significant issues pertaining to such factors as future fertility and the development of a potentially life-threatening disease in a previously healthy, productive individual. These issues need to be taken into account in overall patient management.

The incidence of testicular cancer has gradually increased over the last 25 years, from 2.3 cases per 100,000 men in 1964 to 4 per 100,000 men in 1993; this trend is due mainly to an increased incidence in white males.[1,2] Thirty years ago, testicular cancer accounted for 11.4% of all cancer deaths in the 25- to 34-year-old age group, with an overall 5-year survival rate of 64%.[3] In 1994, the cure rate for testis cancer approached 100%. Improved diagnostic techniques and tumor markers, as well as effective platinum-based multidrug chemotherapeutic regimens, have combined to significantly reduce patient morbidity and mortality.

In addition, modifications in the surgical management of testicular cancer have significantly lowered...
the morbidity associated with the classic full bilateral retroperitoneal lymph node dissection (RPLND), which was routinely performed prior to the early part of the 1980s. This advance, combined with the fact that approximately 30% to 50% of patients with a clinical stage I nonseminomatous germ cell testicular tumor (NSGCT) actually have pathologic stage II disease, has made surgery an important treatment option for both physicians and patients.

Retroperitoneal lymph node dissection not only is an important component of the management of patients with low-stage NSGCT but also has a major role in the management of residual disease following chemotherapy. Approximately 30% of patients who are initially treated with chemotherapy are found to have a residual mass at follow-up. Removing this mass restages the patient and, in cases where persistent carcinoma exists, the physician is alerted to the need for further management.

Therefore, as will be discussed below, RPLND plays a role in both low- and high-stage disease. It is a well-defined, reproducible surgical procedure with low morbidity, which benefits the patient in terms of both allowing for accurate pathologic staging and providing a surgical cure.

Natural History of Testicular Cancer

Clinical observation of patients with testicular cancer has led to an understanding of its local growth characteristics, as well as its patterns of spread. Following malignant transformation of the germinal epithelium, tumor growth initially tends to remain confined to the testis itself, as the tough fibrous tunica albuginea offers a degree of protection to the epididymis. The tumor gains access to the lymphatics at the testicular mediastinum. FIGURE 1

Lymphatic Drainage

With the notable exception of choriocarcinoma, germ cell testicular neoplasms spread in a predictable, stepwise fashion. The lymphatic drainage of the testicle has been well documented by both surgeons and anatomists. One of the first experimental studies of testicular lymphatics was performed in 1910 by Jamieson and Dobson. Apart from their important contribution in defining lymphatic drainage of the testicle, these authors correctly pointed out that in order to cure testicular cancer, complete removal of the "retroperitoneal lymphatic area" was necessary; however, they felt that this procedure was exceedingly difficult and dangerous, if not impossible! FIGURE 2

Nodal Metastases

The spermatic cord contains four to eight lymphatic channels that ascend into the retroperitoneum and fan out medially into the retroperitoneal lymph node chain. The first echelon of lymph nodes draining the right testis is located within the interaortocaval nodes, at the level of the second vertebral body. The first echelon of nodes draining the left testis is located in the para-aortic region.
in an area bounded by the renal vein superiorly, the aorta medially, the ureter laterally, and the
origin of the inferior mesenteric artery inferiorly. Following spread of germ cell neoplasms to either
the left or right primary echelon of nodes, subsequent metastasis may occur in a retrograde fashion
to the common external and inguinal nodes, or cephalad via the cysterna chyli, thoracic duct, and
supraclavicular nodes (Figure 2).

In a review of 104 consecutive patients with stage II (B) NSGCT, Donohue et al[8] made a number of
important observations confirming the predictable lymphatic spread of testicular tumors. They
reported that suprahilar lymph node spread was extremely rare in stage BI disease but was not
uncommon in stage BII disease. They also confirmed the absence of contralateral node involvement
in low-stage disease when the ipsilateral nodes were negative.[9] In addition, in this series gonadal
vein involvement was noted in a significant number of cases in both low- and high-stage B disease.
Obviously, these observations have important implications for the surgical management of testicular
cancer.

Despite the predictability of lymph node metastasis in testicular cancer, there is a 5% distant failure
rate following node-negative RPLND.[10] This is probably due to the fact that the testicular
lymphatics may very occasionally bypass the retroperitoneal lymph nodes altogether and
communicate directly with the thoracic duct. Lymphatics of the epididymis drain into the external
iliac chain; therefore, in locally extensive disease, epididymal involvement may be associated with
positive pelvic lymph nodes. Testicular cancer that involves the scrotum may result in inguinal node
metastasis; in addition, prior scrotal surgery or retrograde spread from extensive retroperitoneal
involvement may also cause inguinal node metastasis.

Scrotal violation in the setting of orchiectomy for testicular cancer has generally been condemned as
compromising patient prognosis. As a result, inguinal orchiectomy with high ligation of the cord has
been the standard of care in the initial management of testicular cancer for almost 100 years.[11]
However, Capelouto et al[12] recently conducted a meta-analysis focusing on the implications of
scrotal violation in patients with testicular cancer. Out of a total of 1,182 patients, scrotal violation
had occurred in 206 patients. No statistical differences in distant recurrence or survival were found,
implying that scrotal violation may not carry a significantly worse prognosis.

In summary, apart from choriocarcinoma, which undergoes both lymphatic and hematogenous
spread at an early stage, germ cell testicular tumors tend to spread, in a predictable fashion, to the
retroperitoneal lymph nodes. Suprahilar involvement usually develops only in higher-stage disease
and, as such, occurs more frequently on the left side than on the right. If the ipsilateral nodes are
negative, the contralateral nodes also are uninvolved. Cross-metastases occur more frequently with
right-sided tumors.

Distant spread of testicular cancer occurs most commonly to the pulmonary region, with
intraparenchymal pulmonary involvement. Subsequent spread is to the liver, viscera, brain, and, late
in the disease course, bone.[13]

This predictable pattern of spread has led to the development of new surgical techniques that
provide both accurate pathologic staging and therapeutic benefit, while at the same time being
associated with minimal morbidity.

**Prediction of Metastatic Potential**

Most patients with NSGCT present with clinical stage I disease. Since 30% to 50% of these patients
may have clinically undetectable metastases, controversy exists as to their subsequent
management.[14,15] In order to offer the patient the highest chance of cure with the lowest possible
morbidity, certain parameters are used to predict the likelihood of metastasis.[16] Factors that
determine the likelihood of relapse in the retroperitoneal nodes, or of late recurrence in clinical stage
I NSGCT, are: the extent of the primary tumor (ie, T-stage), lymphatic or vascular invasion, the
presence of embryonal carcinoma in the primary tumor, and the absence of yolk sac tumor.[17]

Prognostic indices using these risk factors have been developed. As a result of these indices,
patients with clinical stage I NSGCT are no longer managed as a homogeneous group. Rather,
treatment may now be individualized according to the likelihood of positive retroperitoneal lymph
nodes. Patients who are at low risk of having positive nodes may be placed into observation
protocols and thus spared the morbidity of adjuvant therapy. However, despite the prognostic
criteria, it is still not possible to establish highly accurate distinctions between patients who should
and should not receive adjuvant therapy. In this regard, the Medical Research Council study in the
United Kingdom[18] showed that the high-risk group constituted fewer than 25% of patients with
testicular cancer and accounted for less than half of the relapses.
Staging of Testicular Cancer

TABLE 1

Clinical Staging Systems for Testicular Cancer

Both clinical and pathologic staging systems for NSGCT have been developed (Table 1 and Table 2). Since therapies differ for seminoma and NSGCT, there are separate staging systems for these two entities. Although numerous staging systems are currently employed, the majority are a variation on the system proposed by Boden and Gibb in 1951.[19] It is important to note that the measurement of the size of involved lymph nodes in the Memorial Sloan-Kettering Cancer Center system refers to the total diameter of all enlarged lymph nodes, not to the diameter of the largest lymph node. Low-stage disease includes stages I (A) and IIA (B1) disease, whereas high-stage disease encompasses stages IIB (B2), IIC (B3), and III (C) disease. This distinction between low- and high-stage disease is important, as it determines, to a large degree, what type of adjuvant therapy the patient receives and also is used to evaluate the results of various treatment protocols. TABLE 2

Pathologic Staging Systems for Testicular Cancer

The clinical staging systems are based on noninvasive diagnostic techniques, whereas pathologic staging is based on the specimens obtained at radical orchiectomy and RPLND (Table 2). The staging error which is associated with clinical staging is therefore removed.

Staging Work-up

Following radical orchiectomy and evaluation of the primary tumor, the staging work-up for metastatic disease commences. The primary landing sites for metastatic disease in the retroperitoneum have been well described (Figure 2). Prior to the development of CT, the retroperitoneum was assessed by a combination of physical examination, intravenous pyelography, and bipedal lymphangiography. Due to the low yield and potential morbidity of lymphangiography,[20] this technique has been abandoned in the work-up of NSGCT. Computed tomographic scanning is currently the imaging modality of choice for the retroperitoneum in patients with germ cell testicular tumors. Since the CT scan cannot detect the presence of micrometastases, it is associated with a significant false-negative rate: 44% in a study by Richie et al.[21] and 59% in a report by MacLeod et al.[22] In general, the accuracy of CT scanning of the retroperitoneum is 68% to 90%.[23-25]

Improved diagnoses with newer generations of scanners and techniques have not led to a significant decrease in false-negative rates. Therefore RPLND remains the gold standard for staging patients with NSGCT and, as such, has the advantage of detecting micrometastases in patients who would otherwise have been placed on an observation protocol (which would be destined to fail). In addition, it provides a surgical cure in a significant subset of patients.

Fertility in Patients With Testicular Cancer
Fertility is one of the most important issues in patients with NSGCT. In this regard, it needs to be borne in mind that the preservation of ejaculation is not synonymous with achieving pregnancy.[26] In fact, approximately 40% to 70% of patients are hypofertile, at least temporarily, after orchiectomy for testicular cancer.[27] This may be due to a variety of factors, such as the association of cryptorchidism with testicular cancer, stress, and the surgical trauma to one testicle, which may have an effect on the contralateral testicle.[28] In addition, higher concentrations of antisperm antibodies are present in patients with testicular cancer than in the normal population.[29] In a significant percentage of these patients, semen analyses will improve after therapy. Nevertheless, an estimated 25% of patients will have a persistent subfertile pattern on semen analysis.[30] Thus, only 75% of patients with NSGCT have fertility that can be preserved.

The best measurement of fertility is pregnancy. A retrospective review of the Indiana University experience in 201 patients with clinical stage I disease NSGCT showed that, of 66 patients who attempted to achieve a pregnancy after RPLND, 50 (76%) were successful.[31] Also, Mansen et al have studied paternity in patients treated with chemotherapy for testicular cancer.[32] In this study, three of eight patients who attempted pregnancy after platinum-based chemotherapy were successful.

Retroperitoneal Lymph Node Dissection

RPLND has evolved considerably since the early 1900s when the technique was first performed. Bilateral dissections, which became standard therapy for low-stage testicular cancer in the 1950s and ‘60s, gave way, in the 1980s and ‘90s, to less extensive, template and nerve-sparing techniques. Currently, the type of dissection performed varies, depending on which disease stage is being treated.

RPLND-I—This dissection is performed in patients with no clinical signs of spread to the retroperitoneum and no surgically visible disease, ie, clinical stage I disease. The surgical technique employed is either the template or nerve-sparing technique. In the modified template technique, the dissection is complete above the level of the inferior mesenteric artery but is limited to the ipsilateral side below the level of the inferior mesenteric. In the nerve-sparing RPLND, the lumbar sympathetic nerves are prospectively identified and preserved, and the node-bearing tissues around these nerves are then removed. Both techniques preserve ejaculation in the vast majority of patients.

RPLND-II—This is performed in patients with low-volume, clinically demonstrable disease or with visible disease at surgery, ie, clinical stage IIA or IIB disease. The surgical boundaries are generally wider than in RPLND-I, are usually bilateral above the inferior mesenteric artery, and, in most cases, are bilateral below the inferior mesenteric artery as well. The lumbar sympathetic nerves and the hypogastric plexus are carefully preserved, resulting in preservation of ejaculation in over 95% of patients when the procedure is done by experienced surgeons.

RPLND-III—This is a cytoreductive procedure performed after chemotherapy. Only in highly selected cases are nerve-sparing boundaries utilized. Up to 30% to 50% of patients may have preservation of ejaculation following this procedure.

Management of Clinical Stage I Disease

RPLND-I vs Surveillance

The decision to place a patient on a surveillance protocol or to perform RPLND depends on a number of factors, such as T-stage, tumor histology, presence of vascular or lymphatic invasion, and patience compliance. Local expertise in performing RPLND is also an important factor. There are a number of fundamental reasons for advocating RPLND in clinical stage I disease: Approximately 30% of patients who present with clinical stage I NSGCT actually have pathologic stage II tumors. By performing RPLND in this subset of patients, their more extensive disease will be recognized earlier in the disease course. Testicular cancer is no exception to the general rule that when a cancer is discovered early, not only is treatment better tolerated and less severe but also the chance for cure is that much greater. Accurate pathologic staging allows for earlier definition of treatment requirements. For example, patients found to have pathologic stage II disease can be given the option of two courses of chemotherapy.[33] If, on the other hand, these patients are placed on a surveillance protocol and suffer a subsequent clinical recurrence, three to four courses of chemotherapy would be required, with attendant increases in short- and long-term morbidity.

Retroperitoneal lymphadenectomy not only is a staging procedure but also is a therapeutic procedure.
Donohue et al reviewed their 25-year experience with RPLND in 464 patients with clinical stage A disease. Among the patients in whom pathologic stage II disease was detected at RPLND, 65% did not relapse.[34] Therefore, a significant number of patients with low-stage II disease are cured by RPLND alone and do not require subsequent adjuvant chemotherapy or radiotherapy. Follow-up after RPLND is simple and efficient. Patients are followed with chest x-rays and tumor marker determinations. Also, relapse is rare, is usually in the chest when it does occur, and virtually 100% of patients who suffer a recurrence are curable with chemotherapy.[35] Retroperitoneal lymphadenectomy eliminates the source of concern that most patients on surveillance protocols inevitably feel; namely, that metastatic testicular cancer is being managed conservatively.

Significant cost savings can be effected with RPLND due to the fact that follow-up does not include frequent expensive imaging studies, as is the case with patients on surveillance protocols. Despite the obvious advantages of RPLND in clinical stage I disease, the procedure does have drawbacks. The major disadvantage is the fact that 70% of clinical stage I patients do, in fact, have pathologic stage I disease, and therefore, are subjected to an unnecessary major surgical procedure, with its attendant morbidity. In centers of surgical expertise, RPLND carries a very low morbidity, and mortality approaches zero.[35,36] The average patient undergoing RPLND-I is under anesthesia for less than 3 hours, requires no blood transfusions, and is hospitalized for 5 to 7 days. Resumption of limited employment and moderate activity can occur within 2 weeks, and a return to full activity normally is possible within 4 to 6 weeks.[37] Fewer than 1% of patients develop the long-term morbidity of small bowel obstruction due to adhesions.[38]

Despite the fact that morbidity associated with RPLND-I is low, the need to identify patients with clinical stage I disease who are likely to harbor occult metastases is apparent and remains the subject of ongoing studies. Albers et al[39] recently reported on the use of flow cytometry and single-cell cytophotometry in the prediction of metastases. They demonstrated that high proliferative activity, as measured by S- and G2M-phase analysis, was an important risk factor for occult metastatic disease.

Although surveillance may be a good approach for patients who do not relapse, it carries a distinct disadvantage for those who relapse in the retroperitoneum and chest as late as 4 years or more after orchiectomy. The majority of this subset of patients will be subjected to three to four cycles of chemotherapy with the possibility of resection of a residual mass following chemotherapy. Thus, both the short- and long-term morbidity of chemotherapy, needs to be weighed against the very low morbidity associated with RPLND-I. Furthermore, relapses carry a high mortality.

In addition, rigid compliance to the follow-up protocol is necessary. Peters studied the impact on clinicians of entering patients into surveillance protocols.[40] He reported that a busy clinician may not be able to adequately follow more than 25 patients on a surveillance protocol without the help of a data manager.

The completeness of RPLND is critical. Donohue et al[41] reported that none of their 464 patients who underwent RPLND for clinical stage I disease relapsed in the retroperitoneum. Baniel et al[42] recently described a series of 35 patients initially diagnosed with low-stage NSGCT who presented with late (more than 2 years following initial management) relapse. A total of 31 patients were initially treated with RPLND, 19 of whom developed a retroperitoneal recurrence. Despite the fact that this subset had received chemotherapy following RPLND, 58% relapsed, implying that node dissections were inadequate and that residual tumor may have transformed into a far more resistant tumor. In other words, inadequate RPLND for low-stage disease cannot be compensated for by subsequent adjuvant chemotherapy.

**Approach Used at Brigham and Women's Hospital**

At the Brigham and Women's Hospital, we generally reserve RPLND-I for patients with high-risk clinical stage A nonseminoma. We define high-risk disease as: embryonal carcinoma more than 40% of tumor volume, any T-stage greater than T1, and any vascular or lymphatic invasion. All other patients are given the option of surveillance.

We prefer the modified (template) technique, and generally use a mid-line transabdominal approach. Thus, a complete bilateral dissection is performed in the area most likely to contain positive lymph nodes, while the nerves controlling ejaculation are spared.

**Summary**

In summary, RPLND-I is generally performed for high-risk clinical stage I disease. This procedure accurately stages the tumor and offers the patient the likelihood of a surgical cure. In addition,
RPLND-I carries a very low risk of short- and long-term morbidity. Nevertheless, patient selection needs to be improved, and, in this regard, further research is required.

Management of Clinical Stage II Disease

The most appropriate form of therapy for patients with clinical stage II NSGCT is an area of ongoing debate. This controversy centers on: (1) the role of adjuvant chemotherapy following RPLND and (2) surgery vs chemotherapy as initial treatment.

Retroperitoneal lymph node involvement in patients with NSGCT, as detected by CT scan, is classified as being less than 2 cm (stage IIA), between 2 and 5 cm (stage IIB), and more than 5 cm in diameter (stage IIC). There is general agreement that clinical stages IIC and III disease should be managed initially with chemotherapy, and that surgery should be reserved for residual retroperitoneal masses. However, the initial management of clinical stages IIA and IIB disease remains controversial.

Role of Adjuvant Chemotherapy

The 2-year disease-free survival rate for patients with pathologic stage II NSGCT following RPLND is 60% to 80%, indicating a 20% to 40% incidence of recurrence, which is usually in the lungs. The role of adjuvant chemotherapy following RPLND, vs an expectant approach with chemotherapy administered at the time of recurrence, has been addressed by several authors.[43,44] A randomized multicenter study by Williams et al[45] reported a 48% relapse rate for patients with positive nodes who were observed following RPLND-II. In contrast, the relapse rate in patients who received 2 cycles of adjuvant chemotherapy following RPLND was 2%. This study included all patients from stage N1 to N3 with positive nodes. There were no statistical differences in the relapse rate among patients with various nodal stages.

In contrast, Richie and Kantoff[43] reviewed 39 patients with pathologic stage II disease who were carefully followed after RPLND-II. Relapses occurred in only 8% of patients, all of whom were rendered disease free with three to four cycles of chemotherapy. In other words, immediate post-RPLND chemotherapy would have benefited only a relatively small number of patients. This study highlights the fact that results from institutions where RPLND is performed frequently may not parallel results from large cooperative trials, in which some centers contribute relatively small numbers of patients.

In general, relapse rates for pathologic stage II disease resected by RPLND have ranged from 30% to 70%.[43] As with clinical stage I disease, the question of overtreatment of clinical stage II disease has been raised. Thus, several reports have focused on the risk factors associated with a high likelihood of recurrence following RPLND for clinical stage II disease. Javadpour and Young[46] noted increased relapse rates in patients with more than five positive lymph nodes or any lymph node more than 2 cm in diameter and whose tumor displayed vascular invasion or was predominantly embryonal in nature.

Following RPLND-II, the decision to give two cycles of adjuvant chemotherapy depends largely on the tumor volume and number of positive lymph nodes, as well as on the histopathology of the primary tumor. Expectant management is appropriate in patients with fewer than six positive nodes (all of which are less than 2 cm in diameter) and no positive margins.[39] For patients with more than six positive nodes or high-volume disease, two cycles of chemotherapy are given following RPLND; this protocol has achieved excellent cure rates.[47] For patients who develop a recurrence while being treated expectantly, chemotherapy is employed at that stage, once again with excellent remission rates.

Approach Used at Brigham and Women's Hospital

At Brigham and Women's Hospital,[46] most patients presenting with clinical stage IIA disease are treated with RPLND-II. Patients with &pound; 3 cm of nodal involvement are offered RPLND, and for those with more than 3 cm of nodal involvement, chemotherapy is generally recommended. This approach often obviates double therapy. For patients with stage IIB disease and unfavorable histology (teratomatous elements), RPLND is generally preferred, whereas for patients with pure embryonal stage IIB disease, chemotherapy is offered as first-line adjuvant therapy. In patients with persistent tumor markers following radical orchiectomy and no evidence of retroperitoneal involvement, chemotherapy is the initial treatment of choice. All patients with stage IIC disease are scheduled to receive initial chemotherapy.
When suspicious lymph nodes are encountered at RPLND, we proceed with a complete bilateral node dissection; for patients with palpable disease, the dissection also includes the suprahilar regions. A mid-line transabdominal approach is preferred for right-sided tumors, whereas a thoracoabdominal approach is used for left-sided tumors. In patients with evidence of low-stage retroperitoneal involvement and positive tumor markers following radical orchiectomy, we perform a bilateral complete RPLND.

**Summary**

Clinical stage II NSGCT can be managed in a variety of ways, depending on the tumor burden, histopathology, level of surgical expertise, and the patient's desires. The potential advantage of RPLND is that it can eradicate disease in over 50% of patients with NSGCT. Patient compliance and meticulous follow-up will usually ensure a successful outcome.

**Management of Clinical Stage III Disease**

**Rationale for RPLND-III**

In patients with advanced NSGCT, adjunctive surgery plays an important role in assessing response to chemotherapy, resecting persistent germ cell tumor, and defining the need for further therapy. At institutions where RPLND-III is performed for residual disease only, three subsets of histopathology have been observed: necrosis/fibrosis (40%), adult teratoma only (40%), and residual NSGCT (20%). Thus, approximately 60% of patients with evidence of a residual mass on post-chemotherapy imaging studies have either viable cancer or teratoma. The criteria for RPLND-III are controversial, and there are no clear guidelines for its use. The presence of elevated tumor markers after chemotherapy, however, remains the only generally accepted contraindication to adjunctive surgery.[49] The management of patients whose tumor markers normalize following chemotherapy ranges from observation for all patients, irrespective of the findings of the imaging studies, to surgery for all patients.[50,51]

A significant number of patients with normal CT scans following chemotherapy, in fact, have viable tumor in the retroperitoneum. Richie reported viable germ cell tumor in 11 of 38 patients who underwent adjunctive surgery following four cycles of chemotherapy.[52] However, the definition of a "normal" CT scan differs from one institution to another. Definitions include: no visible mass, lymph nodes no larger than 1 cm, and lymph nodes less than 1.5 to 2 cm in greatest diameter.[43] RPLND-III is a very demanding procedure technically, and complication rates ranging from 6% to 8% have been reported. In view of this, several investigators have attempted to identify patients in whom RPLND-III can be omitted. Among patients with no teratomatous elements detected in the primary tumor and a ≥90% decrease in the volume of retroperitoneal disease on sequential CT scans, Donohue and Rowland[53] found no teratoma or viable germ cell tumor elements in the resected specimen. On the other hand, Loehrer et al[54] reported that in 51 patients with teratoma found at post-chemotherapy resection, 28% of the primary specimens did not contain teratomatous elements.

While there are statistical correlations between various factors, such as degree of tumor shrinkage, size of residual mass, prechemotherapy tumor markers, teratomatous elements in the primary specimen, and the histology of the resected specimen the risk of a false-negative prediction is approximately 20%.[55] This false-negative rate has important implications due to the fact that teratoma has the ability to grow rapidly and become unresectable. In addition, disease-free survival following RPLND-III for teratoma depends on the completeness of resection, and thus, early resections of teratoma are associated with the best possible chance of long-term disease-free survival.[56] Finally, there is a risk of malignant transformation of teratoma, ie, the development of sarcomatous and nongerminial carcinomatous malignant elements.

**Approach Used at Brigham and Women's Hospital**

At the Brigham and Women's Hospital, RPLND-III is performed in all patients with positive CT scans (visible mass) post-chemotherapy and in those whose primary tumor contained teratomatous elements. In patients with pure embryonal primary tumors who have a residual retroperitoneal mass of less than 2 cm following chemotherapy, an observation policy is adopted. We feel that the modified/nerve-sparing procedures are an unacceptable compromise in patients with residual disease following chemotherapy, especially in those with frozen-section evidence of a germ cell tumor. Thus, we do not routinely employ these techniques as part of the RPLND-III.
Patients exposed to bleomycin (Blenoxane) are carefully monitored during surgery. Also in such patients, the inspired concentration of oxygen is reduced, intraoperative and postoperative fluid replacement is limited, and colloid solutions are used in place of crystalloid solutions. For patients with bulky disease, we prefer a left thoracoabdominal approach, through the bed of the eighth or ninth rib. However, for large retrocrural or posterior mediastinal disease, a higher thoracotomy or median sternotomy may be necessary. Patients with bulky teratoma may require resection in stages; eg, chest followed by abdominal resection. Bulky retroperitoneal disease mandates complete excision of all tissue, a procedure that is extremely challenging. Consequently, this procedure should be performed only by surgeons with the appropriate expertise. Residual disease composed of germ cell tumor elements is managed with another two cycles of salvage chemotherapy. If only teratoma or necrosis is detected, we require that patients receive chest and abdominal CT scans every 6 months, together with chest radiographs and serum tumor markers every 2 months.

**Summary**

The surgical management of patients with evidence of residual disease after chemotherapy for NSGCT is both controversial and challenging. Management is based on post-chemotherapy imaging studies, as well as on primary tumor histology. In view of the fact that these cases are extremely challenging, they should be managed in centers where the necessary skills are available.

**Conclusions**

Tremendous advances have been made in the management of germ cell testis tumors during the 20th century. With a multimodality approach, testicular cancer is curable in the vast majority of cases. In addition, refinements in treatment modalities have minimized patient morbidity without compromising disease-free survival rates. Retroperitoneal lymph node dissection not only provides accurate data for pathologic staging but also is therapeutic in low-stage disease. Moreover, RPLND also plays an essential role in the management of high-stage disease, with respect to both directing further patient management and providing long-term disease-free survival following complete resection of residual teratoma. Precise surgical technique is mandatory to ensure disease-free survival. Further improvements in the management of testicular cancer will come from better selection of low- and high-stage patients for adjuvant therapy. Genetic analysis of germ cell tumors may play a role in this regard.

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