Role of Retroperitoneal Lymph Node Dissection in the Management of Testicular Cancer

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Retroperitoneal lymph node dissection for management of testicular cancer at various stages is reviewed.

Background: Retroperitoneal lymph node dissection is an important component of staging and management of nonseminomatous germ-cell carcinoma of the testis. Ejaculatory impotence has been a dominant aspect of operative morbidity.

Methods: The author has led the investigation of a series of modifications of operative techniques with the aim of reducing morbidity while retaining the prognostic and therapeutic benefits for retroperitoneal lymph node dissection.

Results: The advances in surgical techniques have reduced the incidence of ejaculatory impotence to less than 5%. Guidelines for the type of retroperitoneal lymph node dissection for different clinical stages of disease are presented.

Conclusions: The advances in surgical techniques for retroperitoneal node dissection have minimized morbidity. The procedure plays a role in many clinical stages of testicular cancer.

Introduction

The lymphatic drainage of the testis was studied by Jamieson and Dobson[1] in 1910. Based on the knowledge of the lymphatic distribution, Cooper et al[2] performed retroperitoneal lymph node dissections (RPLNDs) on patients with testicular cancer in the 1950s, and this technique was then studied and expanded by Donohue.[3] In early experience, the extent and thoroughness of the dissection increased based on observations of occasional involvement of suprahilar left periaortic and interaortocaval nodes in patients with low-volume disease. The suprahilar zones were routinely resected as well as all of the node-bearing tissue between the ureters from the renal vessels to the bifurcation of the common iliac arteries. Donohue described a “split and roll” technique to ensure clearance of the nodal tissue completely around the great vessels. This technique of extended RPLND was used for patients with low-stage clinical disease as primary treatment and for patients who had presented with advanced stage and/or bulky retroperitoneal metastases who did not achieve a complete remission with chemotherapy.

Approximately 60% of patients with low-stage clinical disease who had pathologically positive nodes were rendered disease-free by RPLND alone.[4,5] In patients with pathologically negative nodes, only 5% to 10% relapsed at a later time. Relapses in the retroperitoneum were rare and were detected early by elevation of serum markers or by chest radiographs. The subsequent salvage rate with chemotherapy was virtually 100%.[4]

Evolution of Surgical Technique

By the early to mid 1980s, many investigators were attempting to modify the RPLND technique to decrease or eliminate ejaculatory impotence, a major side effect in this population of young patients. Ejaculatory impotence, which causes infertility, is a result of the resection of the lumbar sympathetic chains and/or the postganglionic branches of the lumbar sympathetic nerves. Fig 1 shows the course of the lumbar sympathetic chains and their postganglionic branches. Initial attempts at sparing the lumbar sympathetic chains involved modifying the template of the dissection based on whether the primary tumor is left- or right-sided.

A study performed at Indiana University Medical Center[6] described the distribution of positive lymph nodes by the size and total number of nodes involved and by the location of the tumor. These data showed that in clinical stage I patients, nodal involvement was highly predictable as to the location of positive nodes. A rationale for altering the templates of dissections was based on this study. Figs 2A and B show the margins of dissection for the modified templates for right- and left-sided tumors.
In patients with right-sided tumors, the left periaortic and presacral zones were spared, as well as the suprahilar zones. This modified template spared the left lumbar sympathetic chain and the postganglionic branches connecting to the sacral plexus. At our institution, preservation of emission was seen in 94% of patients having a right-sided, modified template en bloc dissection. For left-sided tumors, the right pericaval and presacral zones were spared along with the suprahilar zones. Approximately half of the patients had preservation of emission using this template with an en bloc dissection with division of the inferior mesenteric artery. Once the technique was modified to spare the inferior mesenteric artery and the adjacent neural tissue, the results improved to 83% with preservation of emission. This is most likely due to preservation of the right lumbar sympathetic chain and its lower postganglionic branches. Subsequent modifications in technique include utilizing the same templates as the modified in block techniques shown in Figs 2A and B but with the application of a “split and roll” sympathetic nerve-sparing technique. All nodal tissue within these templates is removed, but the sympathetic nerves are spared. These modifications have resulted in an increase in the preservation of ejaculatory emission to over 95%.[7]

Table 1 presents the relapse rates at Indiana University Medical Center in clinical stage I patients according to pathologic stage and type of RPLND performed. These data do not show any significant increase in relapse rate with the modified template or nerve-sparing techniques. Based on these findings, these techniques are used in the majority of patients with clinical low-stage disease who are concerned about fertility. If fertility is not an issue for a patient with clinical low-stage disease, the modified template en bloc technique is used since nerve-sparing techniques are more time consuming. In advanced disease, the full bilateral RPLND has been used. The limits of dissection are shown in Fig 3.

**RPLND in Clinical Low-Stage Testicular Cancer**

**Clinical Stage I**

Patients with clinical stage I cancer of the testis are defined as those with no evidence of visceral, retroperitoneal, chest, or mediastinal metastases by computed tomography scans. Serum alpha-fetoprotein (AFP) or beta-human chorionic gonadotropin (Beta-HCG) elevation must be decreasing after orchiectomy at the expected rate, based on the half-lives for these markers of five days and one day, respectively.

A 1982 study at Indiana University Medical Center[8] showed that the accuracy of staging clinical stage I and II patients was 70%, with 75% of the clinical stage I patients being staged correctly. In a larger study at the same institution, the overall relapse rate of pathologic stage I patients after RPLND was 11%. [5] The overall survival of clinical stage I patients who were pathologic stage II since the advent of adjuvant therapy has been 100%. [5] Despite this high success rate, other centers initiated surveillance studies in an attempt to reduce the overall treatment rate of patients and to spare patients the potential morbidity of ejaculatory impotence (before the prospective nerve-sparing techniques were developed and their efficacy was proven).

Attempts have been made to define risk factors for identifying those patients at a high risk for metastases even when all clinical testing for metastases is negative. Vascular or lymphatic invasion of the tumor, the presence of teratoma,[9] and a high percentage of embryonal cell carcinoma have been considered to be risk factors for metastases. Albers and associates[10] recently completed a prospective study using flow cytometry to identify patients at high risk for metastases. Those patients with high percentages of cells in the S or the G2M phase had significantly higher risk of metastases.

A recent surveillance study[11] with a 10-year follow-up for clinical stage I nonseminomatous germ cell tumor of the testis (NSGCTT) provided information on 85 NSGCTT patients. The overall relapse rate of clinical stage I patients followed by surveillance was 29.4%. Relapse occurred at a median of seven months after orchiectomy (range 2-68 months). Of the 25 patients who relapsed, 14 (56%) relapsed in the retroperitoneum (11 in the retroperitoneum alone and three in the retroperitoneum and lung). Half of the retroperitoneal relapses and only one of the 11 lung relapses were larger than 5 cm at detection. The median time of detection of retroperitoneal and lung relapses was 12 months and four months, respectively. Overall, three of the 25 patients who relapsed died of disease (3.5% of the original population).

Based on these data, primary RPLND for patients with clinical stage I NSGCTT is still recommended at our center. The low mortality rates (0.8%) for treatment and disease justify this procedure for all patients when the nerve-sparing technique is used for those interested in fertility.

**Clinical Stage II**

Early experience at our institution showed that 60% of patients with clinical stage II disease could achieve a complete remission by primary RPLND alone. The risk of relapse was directly related to the volume of retroperitoneal metastases. As a result, those patients with bulky retroperitoneal metastases (6 cm or larger, clinical stage IIC) were treated with chemotherapy first. Approximately 80% achieved a complete remission with monotherapy (primary chemotherapy) alone.[12]

Swanson et al[13] reported a series of clinical stage II patients with NSGCTT that contained teratoma in the primary specimen. They concluded that RPLND should be the primary treatment in this patient population since the need for dual therapy was approximately 38% regardless of whether chemotherapy or RPLND was used as the primary treatment. Also, the morbidity and mortality of RPLND are decreased in the primary setting compared with the postchemotherapy setting.

Although false-positive results can occur for clinical stage II patients,[8] primary RPLND is still recommended at our institute for clinical stage IIA (marker elevation persistent after orchiectomy with no abnormalities on computed tomography scan) or clinical stage IIB (retroperitoneal nodal masses up to 6 cm by computed tomography scan). Depending on the distribution and extent of disease, limited templates and prospective nerve-sparing techniques of RPLND still may be used.

**RPLND in Clinical Advanced-Stage Testicular Cancer**

Patients presenting with bulky retroperitoneal (stage IIC) and/or disseminated disease (stage III) usually are treated with primary platinum-based combination chemotherapy. The likelihood of achieving a complete remission is inversely related to the volume of tumor present and the presence of teratoma in the primary tumor. [13] Traditionally, postchemotherapy RPLND was used for patients who did not achieve a complete remission by computed tomography findings but had normalization...
in tumor markers. Donohue et al.[14] reported that patients with a decrease of more than 90% in their retroperitoneal metastases, with a normalization of serum markers, and with no teratoma in the primary tumor can be observed rather than treated with lymphadenectomy, due to the low probability of any significant pathology (ie, teratoma or carcinoma) in the residual masses.

Although the morbidity and mortality are higher with postchemotherapy RPLND than with the primary RPLND,[15-17] this procedure still can be performed safely. The value of RPLND in rendering many patients who achieved only partial remission with primary chemotherapy has been recognized since the early platinum data were reported in the late 1970s.[4] Over the next 20 years, the role of RPLND has changed only slightly in this context. Based on studies[18] showing that the distribution of nodes containing residual cancer or teratoma was not predictable (as was the case in low-stage disease).[6] full bilateral templates usually have been used. Recently, nerve-sparing techniques have been applied when possible. If the retroperitoneal disease has been confined to just one area (eg, the left periaortic or interaortocaval zones), nerve-sparing techniques are used in the remaining zones. Depending on the findings at the time of RPLND, including the degree of induration and matting of tissue around the sympathetic nerves, it may even be possible to preserve nerves in the affected zone.

Postchemotherapy RPLND has been extended to the salvage and desperation cases. A patient who relapsed after primary chemotherapy or remained marker-positive usually was treated with second-line chemotherapy at our center. If the patient failed to achieve a complete remission after second-line chemotherapy, the residual masses were surgically excised, which may have required a thoracotomy in addition to an RPLND.

Due to relatively low salvage rates in patients who have positive markers after primary chemotherapy, salvage RPLND is being used with patients who have discrete and potentially surgically resectable disease. Preliminary experience at this institution shows that this approach appears to yield a higher survival rate in this highly selected population compared with the traditional approach of using second-line chemotherapy with or without autologous bone marrow transplantation (R.G.R., unpublished data, 1996).

Conclusions

RPLND has evolved in its techniques and applications. To prolong survival while minimizing the extent, morbidity, and mortality of treatments used for patients with testicular cancer, RPLND has been expanded in some areas and decreased in others. Table 2 summarizes the applications of RPLND according to clinical stage and type of procedure. The principal area of morbidity - ejaculatory impotence - has been successfully minimized.

References
