

## Testicular Cancer

## **THE IMPACT OF RESIDUAL EXTRA-RETROPERITONEAL MASSES IN PATIENTS WITH ADVANCED NON-SEMINOMATOUS GERM CELL TESTICULAR CANCER**

*Shayegan B, Carver BS, Bosl GJ, Bajorin D, Motzer RJ, Sheinfeld J*

**INTRODUCTION AND OBJECTIVES:** The integration of chemotherapy and surgical resection of residual masses remains essential in the comprehensive care of patients with advanced non-seminomatous germ cell testicular cancer (NSGCT). We examined the impact of residual extra-retroperitoneal (ERP) masses on cancer progression and survival in patients with advanced NSGCT.

**METHODS:** Between 1989 and 2003, 532 patients with metastatic NSGCT underwent post-chemotherapy retroperitoneal lymph node dissection (PC-RPLND) at our institution. Information was obtained from our prospective surgical database following Institutional Review Board approval. Impact of residual ERP masses on cancer progression and survival was estimated using the Kaplan-Meier method. Cox proportional hazards regression analysis was used to assess the prognostic significance of risk factors for cancer progression.

**RESULTS:** At time of induction chemotherapy, 371 (70%) patients were classified as good-, 68 (13%) as intermediate-, and 89 (17%) as poor-risk by IGCCCG criteria. Among 532 patients, 130 (24%) underwent resection of residual ERP masses, either concurrently with PC-RPLND, or in staged procedures. Histology of ERP masses revealed fibrosis in 86 (66%), teratoma in 31 (24%) and viable germ cell tumor (GCT) in 13 (10%). Concordance with retroperitoneal histology was 83% for fibrosis, 42% for teratoma and 47% for viable GCT. At a median follow-up of 41 months, overall 5-year progression-free probability (PFP) was 83%. In a multivariate analysis of clinical and pathologic variables, IGCCCG risk classification, size of residual retroperitoneal masses, completeness of PC-RPLND and viable GCT in retroperitoneal and ERP residual masses had independent prognostic significance in prediction of cancer progression. In contrast to retroperitoneal teratoma, residual teratoma in ERP masses independently predicted cancer progression. Overall disease-specific survival (DSS) at 5 years was 91%. The presence of viable GCT in ERP masses resulted in death from disease in all but one patient at a median time of 11 months. In contrast, the presence of viable retroperitoneal GCT was associated with a 5-year DSS of 77%. Overall, the presence of ERP masses requiring resection was associated with lower PFP and DSS (5 year PFP and DSS: 74% vs. 85% and 83% vs. 93%, respectively).

**CONCLUSIONS:** Patients with residual ERP teratoma and viable germ GCT are at higher risk of cancer progression and death when compared to those with disease confined to the retroperitoneum

## **LONG-TERM CLINICAL OUTCOME AFTER POSTCHEMOTHERAPY RETROPERITONEAL LYMPH NODE DISSECTION IN MEN WITH RESIDUAL TERATOMA**

*Carver BS, Shayegan B, Serio A, Motzer RJ, Bosl GJ, Sheinfeld J*

**PURPOSE:** The histologic finding of teratoma occurs in approximately 40% of all postchemotherapy retroperitoneal lymph node dissections (PC-RPLND). We evaluated patients at our institution undergoing initial PC-RPLND for teratoma to determine their clinical outcome.

**PATIENTS AND METHODS** We identified 210 patients from 1989 to 2003 with nonseminomatous germ cell tumors (NSGCT) who underwent initial PC-RPLND and were found to have only teratoma in the retroperitoneum. Clinical and pathologic information was obtained from our prospective surgical database, and clinical outcome was reported.

**RESULTS:** Of the 210 patients in our series, 192 (92%) received only induction chemotherapy, and 18 (9%) required additional chemotherapy regimens. PC-RPLND pathology revealed mature teratoma in 178 patients (85%), immature teratoma in 15 patients (7%), and teratoma with malignant transformation in 17 patients (8%). With a median follow-up time for survivors of 37 months, disease recurred in 30 patients. The probability of remaining free of disease recurrence at 5 and 10 years was 83% and 80%, respectively. Of the 30 patients with disease recurrence, 10 (33%) had recurrence with teratoma, five (17%) had recurrence with teratoma with malignant transformation, and 15 (50%) had recurrence with viable germ cell tumor. On multivariable analysis, residual mass size and International Germ Cell Cancer Collaborative Group (IGCCCG) risk classification were predictors of disease recurrence ( $P < .0005$  and  $= .001$ , respectively).

**CONCLUSION:** PC-RPLND remains critical in the management of patients with NSGCT. Patients found to have teratoma at PC-RPLND have a 10-year probability of freedom from recurrence of 80%. The size of the residual mass and IGCCCG risk classification were significant predictors of disease recurrence.

## **PREDICTING TERATOMA IN THE RETROPERITONEUM IN MEN UNDERGOING POST-CHEMOTHERAPY RETROPERITONEAL LYMPH NODE DISSECTION**

*Carver BS, Bianco F, **Shayegan B**, Motzer RJ, Bosl GJ, Sheinfeld J*

**PURPOSE:** The biological potential of teratoma remains unpredictable, therefore identifying its presence in the retroperitoneum remains important. We evaluated patients undergoing post-chemotherapy retroperitoneal lymph node dissection for nonseminomatous germ cell tumors to determine predictors of teratomatous elements in the retroperitoneum.

**MATERIALS AND METHODS:** We identified 532 patients from 1989 to 2003 who underwent retroperitoneal lymph node dissection following chemotherapy for nonseminomatous germ cell tumors at our institution. Multiple clinical and pathological variables were reviewed from our prospective retroperitoneal lymph node dissection database. A logistic regression model was designed based on preoperative variables to predict the presence of teratomatous elements in the retroperitoneal lymph node dissection specimen.

**RESULTS:** Of the 532 patients in our series 450 (85%) received only induction chemotherapy and 82 (15%) required salvage chemotherapy. Teratomatous elements were identified in the orchiectomy specimen in 42% of patients. Retroperitoneal nodal pathology revealed teratomatous elements in 235 (44%) patients and only teratoma in 210 (40%) patients. By multivariate analysis testicular yolk sac tumor ( $p = 0.046$ ), teratoma in the orchiectomy specimen ( $p < 0.005$ ), relative change in nodal size before and after chemotherapy ( $p < 0.005$ ), and no requirement for salvage chemotherapy ( $p = 0.03$ ) were independent predictors for the presence of teratoma in the retroperitoneum.

**CONCLUSIONS:** Teratoma remains a common histological finding in the retroperitoneal lymph nodes following chemotherapy. We have identified several pre-retroperitoneal lymph node dissection variables that predict the finding of teratoma in the retroperitoneum for men treated with chemotherapy for metastatic nonseminomatous germ cell tumors.

**THE INCIDENCE AND IMPLICATIONS OF DISEASE OUTSIDE A MODIFIED TEMPLATE IN MEN UNDERGOING POST-CHEMOTHERAPY RETROPERITONEAL LYMPH NODE DISSECTION (PC-RPLND) FOR METASTATIC NON-SEMINOMATOUS GERM CELL TUMORS (NSGCT)**

*Carver BS, Shayegan B, Motzer RJ, Stasi J, Bajorin D, Bosl GJ, Sheinfeld J*

**INTRODUCTION AND OBJECTIVE:** Modified templates were originally described as a staging procedure to reduce retrograde ejaculation for men undergoing primary RPLND. We evaluated our experience with PC-RPLND to determine the incidence and clinical outcome of men with disease extending outside the boundaries of a modified PC-RPLND.

**METHODS:** From 1989 through 2003, a total of 532 men underwent PC-RPLND for metastatic NSGCT. Of these, 269 (51%) had either viable GCT or teratoma present in the RPLND specimen. Following IRB approval, clinical and pathologic data was obtained from our prospective surgical database. The incidence of disease outside the boundaries of a commonly used modified template was reported. A logistic regression model was constructed to determine predictors for disease outside the modified template. Freedom from disease recurrence was analyzed using the Kaplan Meier Method.

**RESULTS:** Of the 269 patients with viable GCT or teratoma, 86 (32%) had evidence of disease outside the boundaries of a modified template. For left- and right-sided primary tumors disease outside the modified template occurred in 27% and 38% respectively. Patients with positive radiographic imaging outside the modified template had a 69% (24/35) incidence of disease outside the modified template. On multivariable analysis, RP nodal size pre- and post-chemotherapy ( $p=0.002$ ,  $p<0.001$ ), positive radiographic imaging outside the template ( $p<0.001$ ), and clinical stage III disease ( $p=0.027$ ) were independent predictors for the presence of disease outside the modified template. With a median follow-up of 55 months, 59 (69%) remained free of recurrence, 6 (7%) had progressive disease, and 20 (24%) suffered a recurrence. The 5-year probability of disease free survival was 70% for men with disease outside the modified template and 82% for men with disease confined to the modified template ( $p=0.048$ ). The 5-year probability of disease specific survival was 84% for men with disease outside the modified template and 90% for men with disease confined to the modified template ( $p=0.31$ ).

**CONCLUSIONS:** Our data suggests a bilateral RPLND is the prudent approach for the management of men with metastatic NSGCT following chemotherapy since at least 32% of men will have teratoma or viable GCT outside the boundaries of a modified template. The presence of disease outside the modified template is associated with a decreased disease free survival.

## **OUTCOME OF INTERMEDIATE AND POOR-RISK PATIENTS WITH NON-SEMINOMATOUS GERM CELL TESTICULAR CANCER FOLLOWING POST-CHEMOTHERAPY RPLND**

*Shayegan B, Carver BS, Bosl GJ, Bajorin D, Motzer RJ, Sheinfeld J*

**OBJECTIVE:** To evaluate the outcome in patients treated with chemotherapy and retroperitoneal lymph node dissection (RPLND) after an initial diagnosis of International Germ Cell Cancer Collaborative Group (IGCCCG) intermediate- and poor-risk metastatic nonseminomatous testicular germ cell tumour (NSGCT), as the integration of chemotherapy and surgery in managing advanced NSGCT continues to develop.

**PATIENTS AND METHODS:** Between 1989 and 2003, 157 patients initially diagnosed with IGCCCG intermediate- and poor-risk NSGCT had RPLND after chemotherapy at the authors' institution, with a median follow-up of 36 months. Progression-free probability (PFP) and disease-specific survival (DSS) were estimated using the Kaplan–Meier method. Cox proportional hazards regression analysis was used to assess the prognostic significance of risk factors for disease progression after RPLND.

**RESULTS:** In all, 68 (43%) and 89 (57%) patients were assigned as intermediate- and poor-risk, respectively. At the time of RPLND the median residual retroperitoneal mass was 3.0 cm and 29 (19%) men had elevated serum tumour markers ( $\alpha$ -fetoprotein, human chorionic gonadotrophin, or both). Retroperitoneal residual masses were completely resected in 147 (94%) patients; retroperitoneal histology revealed fibrosis in 73 (47%), teratoma in 63 (40%) and viable GCT in 21 (13%). The 5-year overall DSS and PFP were 81% and 70%, respectively. Patients with poor-risk NSGCT were at no greater risk of disease progression than those with intermediate-risk NSGCT. In a multivariate analysis, residual mass size, incomplete surgical resection and the presence of teratoma and viable germ cell cancer independently predicted disease progression after RPLND.

**CONCLUSIONS:** Patients with advanced NSGCT have long-term freedom from disease progression when chemotherapy is combined with resection of residual masses. Our data suggest that the tumour response to chemotherapy, coupled with complete resection of all residual masses, predicts long-term freedom from disease progression.