# Survival Analysis of Pure Seminoma at Post-Chemotherapy Retroperitoneal Lymph Node Dissection

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**Purpose:** Viable seminoma encountered at post-chemotherapy retroperitoneal lymph node dissection for pure testicular seminoma is rare due to the chemosensitivity of this germ cell tumor. In this study we define the natural history of viable seminoma at post-chemotherapy retroperitoneal lymph node dissection.

**Materials and Methods:** The Indiana University testis cancer database was queried from 1988 to 2011 to identify all patients with primary testicular or retroperitoneal pure seminoma and who were found to have pure seminoma at post-chemotherapy retroperitoneal lymph node dissection. Clinical characteristics were reviewed and survival analysis was performed.

**Results:** A total of 36 patients met the study inclusion criteria. All patients received standard first line cisplatin based chemotherapy and 17 received salvage chemotherapy. The decision to proceed to retroperitoneal lymph node dissection was based on enlarging retroperitoneal mass and/or positron emission positivity in the majority of cases. Seven patients had undergone previous retroperitoneal lymph node dissection. Additional surgical procedures were required in 19 patients to achieve a complete resection. The 5-year cancer specific survival rate was 54%. However, only 9 of 36 patients remained continuously free of disease and of these patients 4 received adjuvant chemotherapy. Mean time from post-chemotherapy retroperitoneal lymph node dissection to death was 6.9 months. Second line chemotherapy, reoperative retroperitoneal lymph node dissection and earlier era of treatment were associated with poorer cancer specific survival.

**Conclusions:** A total of 36 patients with pure seminoma were found to have viable pure seminoma at post-chemotherapy retroperitoneal lymph node dissection. While 5-year cancer specific survival was 54%, these surgeries are technically demanding and only a minority of patients achieves a durable cure from surgery alone.

**Key Words:** germinoma, seminoma, lymph node excision

**Abbreviations and Acronyms**

CR = complete response
CSM = cancer specific mortality
CSS = cancer specific survival
DOD = dead of disease
HCG = human chorionic gonadotropin
HDCT = high dose chemotherapy
IU = Indiana University
NED = no evidence of disease
PC-RPLND = post-chemotherapy retroperitoneal lymph node dissection
PET = positron emission tomography
RPLND = retroperitoneal lymph node dissection
STM = serum tumor markers
VeIP = vinblastine/ifosfamide/cisplatin

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Approximately 20% of seminomas are metastatic at presentation. Options for primary management of metastatic disease include external beam radiotherapy or cisplatin based chemotherapy depending on the size and extent of metastases. Seminoma is a particularly chemosensitive tumor with complete response rates of 70% to 90% of patients presenting with metastatic disease.[1–3] All cases are categorized as good risk disease unless nonpulmonary visceral metastases develop.

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Post-chemotherapy residual masses are relatively common after treatment of disseminated seminoma. The management of these residual masses is somewhat controversial given the potential morbidity of retroperitoneal lymph node dissection as well as the low incidence of viable malignancy.[4] Histological examination of residual masses reveals necrosis in 90% and viable malignancy in 10% of cases.[5–7] Some investigators have recommended observing post-chemotherapy masses less than 3 cm in greatest dimension, with surgical resection reserved for well-defined masses 3 cm or greater.[6] Historically the practice at IU has been to observe all patients with residual masses regardless of size, with surgical intervention reserved for those demonstrating serological or radiographic evidence of progression.[8] More recently the use of PET to differentiate viable malignancy from necrosis in patients with seminoma has been the subject of debate.[9,10]

While extensive research has been conducted on the prognostic implications of residual viable malignancy or teratoma at post-chemotherapy RPLND in patients treated with cisplatin based chemotherapy for disseminated nonseminomatous germ cell tumors, the prognosis of viable pure seminoma at PC-RPLND has not been well studied. The largest previous study reported survival outcomes in 6 such patients.[11] In this study we define the clinical behavior of viable seminoma at PC-RPLND.

## PATIENTS AND METHODS

After receiving institutional review board approval, the Indiana University testis cancer database was queried from 1988 to 2010 to identify all patients with a history of primary testicular or retroperitoneal pure seminoma who demonstrated pure seminoma at PC-RPLND. A chart review was then performed to determine pretreatment characteristics, completeness of resection, chemotherapeutic regimens, specific pathological findings and followup data. Patients were contacted by telephone if they had not been seen in the last 12 months. Patients were excluded from analysis if nonseminomatous elements were encountered or if they demonstrated increased alpha-fetoprotein at any point in the treatment course.

Proportions are reported for categorical patient features, and measures of central tendency and dispersion are reported for continuous patient features. Unadjusted Kaplan-Meier survival analysis curves for the primary outcome of cancer specific survival were generated for the entire study group and various patient characteristics with outcomes compared using the log rank test. Followup and CSS were calculated from the date of RPLND. Dying of progressive disease or experiencing treatment related mortality was classified as death events. To ensure those patients lost to followup had not died of disease, their survival was corroborated using the Social Security Death Index. Those lost to followup or dying of unrelated causes were censored at last followup or death, respectively.

Univariate and multivariate Cox proportional hazards regression analyses were used to calculate hazard ratios and 95% CIs to determine independent predictors of CSM. Variables included were age as a continuous variable, clinical stage (II vs III), number of preoperative chemotherapeutic regimens (1 vs 2 or more), retroperitoneal mass size at surgery and increased HCG as continuous variables, reoperative vs primary PC-RPLND and treatment era categorized by 5-year increments.

## RESULTS

A total of 36 patients met inclusion criteria for this study. Median patient age at diagnosis was 36 years and median followup was 69 months (range 1 to 159). Overall 2, 20 and 13 patients presented with clinical stage I, II and III disease, respectively, with staging information missing in 1 patient. One patient presented with International Germ Cell Cancer Collaborative Group intermediate risk disease (skeletal metastases) and all other patients presented with good risk disease. The majority of patients were treated primarily with chemotherapy. All 36 patients received at least induction cisplatin based chemotherapy before referral to IU. Seventeen patients received 2 or more different regimens of chemotherapy before surgical intervention, including 1 who received high dose chemotherapy.

Median time from diagnosis to PC-RPLND was 15 months (range 4 to 50). The indication for RPLND in patients with pure seminoma at IU has traditionally been radiographic or serological evidence of progression after chemotherapy, and this was the indication in 26 patients. PET avidity was the primary indication for resection in 8 additional patients. Information regarding retroperitoneal mass size was available for 5 of these PET avid cases and ranged from 2 to 6 cm. Lastly, 2 patients had primary retroperitoneal seminoma resected for the presence of a residual mass given the potential for sampling error of percutaneous biopsy in categorizing seminomatous or nonseminomatous disease.

Twelve patients had increased HCG at the time of resection. Additionally, 7 patients had undergone previous attempted resections (5) or retroperitoneal biopsies (2). Nineteen patients (51%) had additional surgical procedures at the time of PC-RPLND, including nephrectomy in 11 and inferior vena cava resection or aortic replacement in 7. Two patients undergoing reoperative RPLND had incomplete resections, including 1 with diffuse peritoneal implants noted at attempted surgical resections and 1 with tumor invading the vertebral foramen. The former patient died of progressive disease 3 months after RPLND, and the latter underwent HDCT and was lost to followup.