

# Survival outcomes of postchemotherapy retroperitoneal lymph node dissection for nonseminomatous germ cell tumors: A retrospective cohort study from a single tertiary center in South India

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## ABSTRACT

**Introduction:** Chemotherapy, postchemotherapy retroperitoneal lymph node dissection (pcRPLND), and metastasectomy remain the standard of care for the management of advanced nonseminomatous germ cell tumor (NSGCT).

**Methods:** We retrospectively studied 73 patients who had pcRPLND at a single tertiary-care center (2003–2022). Surgical and clinicopathological features and oncological outcomes are presented.

**Results:** The mean age was 28.27 years (15–48). Three-fourths had Stage III disease at diagnosis. International Germ Cell Cancer Collaborative Group risk stratification was 54.54% and 21.21% in intermediate risk, and poor risk, respectively. Sixty-two patients had Standard, 7 had Salvage and 4 underwent Desperation pcRPLND. Eleven patients (15.06%) required adjunctive procedures. Thirteen patients (17.8%) had  $\geq$  class 3 Clavien–Dindo complications and postoperative mortality occurred in 5 (6.8%) patients. The histopathologies (HPE) of the pcRPLNDs were necrosis, teratoma, and viable tumor in 39.7%, 45.2%, and 15.1%, respectively. Seven patients underwent metastasectomy. An 85% size reduction in the size of RPLN predicted necrosis. There was 71.4% concordance between pcRPLND and metastasectomy HPEs. The median follow-up was 26.72 months (inter-quartile range – 13.25–47.84). The 2-year recurrence-free survival (RFS) rate was 93% (95% confidence interval [CI]–83%–97%) and the overall survival (OS) rate was 90% (95% CI–80%–95%). This is the largest series of pcRPLND for NSGCT in India to our knowledge.

**Conclusion:** Although most of the cohort belonged to stage III, an RFS and OS rate of >90% at 2 years was achieved. We believe that successful management of postchemotherapy residual masses in NSGCT is contingent on the availability of multidisciplinary expertise and is therefore best done at tertiary-care referral centers.

## INTRODUCTION

Testicular cancer is a rare malignancy, constituting <2% of all male malignancies. While the

incidence of the disease is much higher in the Western Hemisphere (~3–7/1,00,000 men per year), the incidence

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in India is much lower with only 0.63/1,00,000 men.<sup>[1]</sup> In India, about 30%–55% of the presenting population have International Union Against Cancer (UICC) prognostic group stage III disease at presentation, of which 20%–37% were of the Intermediate, and 13%–50% were of the Poor International Germ Cell Consensus Classification (IGCCC) prognostic risk groups at presentation.<sup>[2-6]</sup>

Upfront chemotherapy followed by surgery has significantly improved the survival of patients with advanced nonseminomatous germ cell tumors (NSGCTs). Approximately, 30% of patients with NSGCTs have residual masses after chemotherapy; mostly in the retroperitoneum.<sup>[7]</sup> Postchemotherapy residual masses (PCRD)  $\geq 1$  cm need post-chemotherapy retroperitoneal lymph node dissection (pcRPLND) according to current recommendations.<sup>[8-11]</sup> Adjunctive procedures, such as nephrectomy and vascular repair, are sometimes necessary to achieve complete resection and hence, may add morbidity to an already extensive procedure.<sup>[3,12-14]</sup> The decision to perform metastasectomies of significant extraperitoneal residual disease is based on the bulk and the histopathological examination findings (HPE) of the pcRPLND.<sup>[10]</sup> Most patients are referred to our institution for multidisciplinary management of advanced disease. This study aimed to study the clinico-pathological features and surgical and oncological outcomes of patients who underwent pcRPLND for NSGCT.

## MATERIALS AND METHODS

This was a retrospective cohort study, conducted in a single tertiary care center in South India. Patients who had RPLND from January 2003 to December 2022 were screened.

Data including age, primary tumor characteristics including the 2016 Tumor, Node, Metastasis classification of the UICC classification and IGCCC risk groups<sup>[15]</sup> for staging at the time of diagnosis, chemotherapy regimen (first line and salvage), response to chemotherapy according to the RECIST 1.1 criteria,<sup>[16]</sup> and biochemical response using serum tumor markers (STMs) - beta hCG and alpha-fetoprotein, intraoperative and postoperative details, including the type of pcRPLND, HPE of pcRPLND, extra-retroperitoneal metastasectomy details, and the latter's concordance with HPE with the prechemotherapy biopsy and pcRPLND, were acquired from our institutional electronic medical records. This study was approved by our institutional review board.

### Patient selection

Patients who underwent pcRPLND for NSGCT histology of the primary tumor after chemotherapy were included. Females, those who had redo or primary RPLND, or those with HPE other than NSGCT were excluded from the study.

### Perioperative details

Adjunctive procedures were premeditated when preoperative contrast-enhanced computerized tomography (CECT) of the thorax, abdomen, and pelvis (CECT) showed infiltration or complex relation like the encasement of great vessels. In this regard, intraoperative assistance was sought from specialist departments, i.e., usually the hepato-biliary surgeons for liver mobilization and the vascular surgeons for complex vascular reconstruction. Occasionally, a decision to perform an adjunctive procedure was taken intraoperatively when a difficulty was encountered.

All pcRPLNDs were performed by an open approach using a midline laparotomy incision, through the transperitoneal route. The split-and-roll technique was used as necessary. The institutional protocol was to perform a bilateral standard infrahilar template dissection.

Clavien–Dindo classification was used to document postoperative complications.<sup>[17]</sup>

### Follow-up and survival outcome

Follow-up data, including STMs, physical examination, and CECT findings data, were collected at follow-up. These were usually scheduled every 3 months for the first 2 years after surgery, every 6 months in years 3 and 4, and annually thereafter. The final follow-up for this study was done by telephone conversation. Recurrence-free survival (RFS) and overall survival rate (OS) were calculated using the Kaplan–Meier method.<sup>[18]</sup>

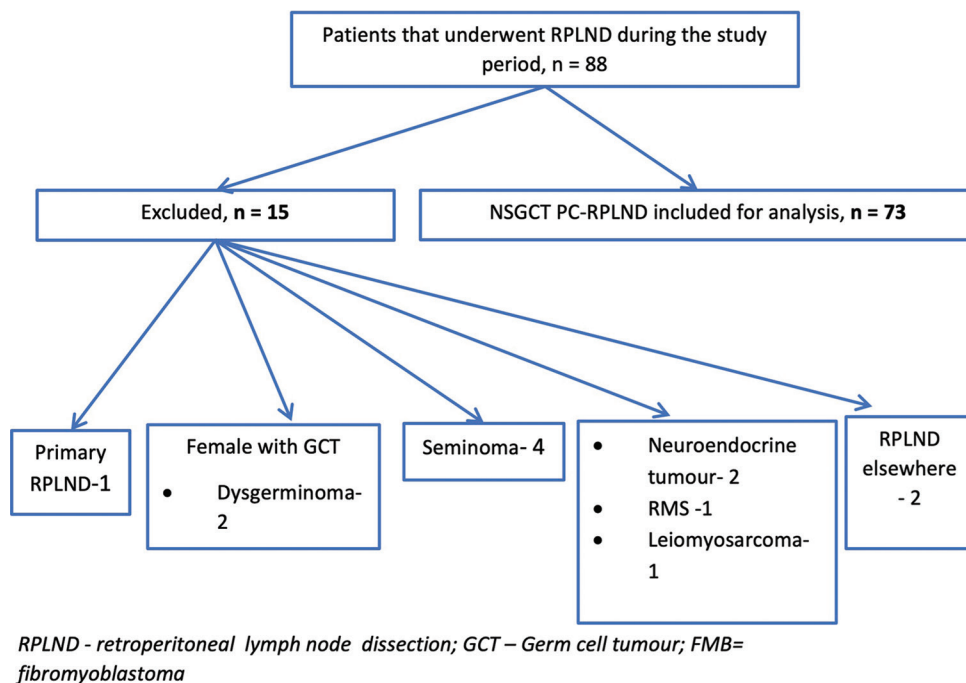
### Statistical methods

Data were summarized using mean (standard deviation)/median (interquartile range [IQR]) for continuous variables and categorical variables, which are expressed as frequency along with percentage. The Kaplan–Meier method was used to estimate the RFS and OS rates. For the analysis of the RFS rate, recurrence was noted as an event. For the analysis of the OS rate, death was noted as the event (defined as death resulting from the disease or its treatments). Those who were alive at their last follow-up or who died of other causes were censored on those respective dates. A receiver operator curve (ROC) was constructed to find the predictive ability of change of size of retroperitoneal mass (pre- and post-chemotherapy) to predict necrosis, and the area under the curve is presented.

## RESULTS

### Patient cohort

Eighty-eight patients underwent RPLND during the study period. Of those, 73 patients fit the inclusion criteria [STROBE diagram illustrating justification for exclusion is shown in Figure 1].



**Figure 1:** STROBE diagram – excluded cases from cohort

### Baseline characteristics

Diagnosis of NSGCT was made before chemotherapy from 53 orchiectomies, 12 retroperitoneal mass biopsies, and 5 supraclavicular mass biopsies. Three patients were diagnosed based on high STMs and imaging alone.

Complete baseline staging data were available for 44 patients. The remaining patients were treated at other medical centers before the RPLND, and reliable baseline staging data were not available. Among them, 33 (75%) patients had stage III and 11 (25%) patients had stage II disease [Table 1].

### Chemotherapy and response details

Regimens executed and the best response to the last chemotherapy are listed in Table 1. First-line chemotherapy was given to 62 patients, and the remaining had additional salvage chemotherapy. The median baseline RPLN mass size (long-axis diameter [LAD]) was 7.5 cm (IQR, 25<sup>th</sup>–75<sup>th</sup> (IQR): 4.6–10.80 cm), and the median size of PCRD was 5 cm (IQR: 2.35–8.0). An ROC curve predicted necrosis with 100% specificity if an  $\geq 85\%$  reduction in the mass size after chemotherapy occurred [Supplementary Appendix Figure 1 depicts ROC prediction of necrosis based on change in LAD].

### Perioperative details

Sixty-two patients had standard, seven had salvage, and four underwent desperation pcRPLND. Seven patients had growing teratoma syndrome (GTS) (six after first-line chemotherapy and one after salvage chemotherapy).

### Adjunctive procedures

Eleven patients (15.06%) required 14 adjunctive procedures [Table 2 shows pcRPLND operative details, including postoperative complications]. Of the 5 (6.8%) adjunctive nephrectomies done, 4 were due to encasement of the kidney and hilum or ureter, and 1 was for nonfunction due to obstruction caused by the mass. Adjunctive procedures were more common with larger retroperitoneal masses (7 [63%] had  $>5$  cm PCRD) or if the mass had teratoma in the final histology (6 [54%] patients). There were 2 (2.7%) separate instances of vascular repair, one that required primary repair of renal artery transection and one that required polytetrafluoroethylene graft replacement of resected aortic wall. All adjunctive procedures were necessary due to dense inseparable adhesions between the mass and the affected adjacent structure that required excision or repair. None of these were due to infiltration on HPE.

### Complications

Eleven patients (15.06%) had  $\geq$  class 3 of Clavien–Dindo postoperative complications. One patient required re-exploration and evacuation of pelvic hematoma later the same day of surgery.

Five patients (6.8%) died within 30 days after surgery. Three (4%) patients died due to postoperative complications. The causes were pulmonary embolism, ventilator-associated pneumonia, and intestinal obstruction, respectively. Two other patients died due to complications related to massive neurological events secondary to intracranial metastases within the first 30 days after pcRPLND. Details of causes of postoperative mortality are documented in Table 2.

**Table 1: Baseline characteristics – demography, primary tumor characteristics, and chemotherapy details**

Baseline characters		Results				
Age (years), mean (SD)		28.27 (7.93)				
Site of testicular tumor, 73 patients, <i>n</i> (%)						
Extragenadal		3 (4.2)				
UDT		3 (4.2)				
Bilateral UDT		1 (1.4)				
Timing of chemotherapy	AFP (ng/mL)	β hCG (IU/L)	LDH (IU/L)			
Prechemotherapy - STM- mean, median (range)	5344, 300 (0.67–65,600) <i>n</i> =49	26,530, 316 (0.10–446,000) <i>n</i> =47	1920, 571 (103–7180) <i>n</i> =44			
Postchemotherapy - STM- mean, median (range)	8, 300 (0.7–82.2) <i>n</i> =70	1.3, 316 (0.10–42.3) <i>n</i> =70	443, 571 (190–1030) <i>n</i> =70			
Histopathology of primary tumor, 73 patients, <i>n</i> (%)						
MGCT		40 (54.8)				
Embryonal carcinoma		15 (20.5)				
Teratoma		8 (10.95)				
Yolk sac tumor		6 (8.2)				
Choriocarcinoma		1 (1.4)				
Diagnosis based on raised serum tumor markers and imaging		3 (4.2)				
UICC prognostic groups, 44 patients, <i>n</i> (%)						
II		11 (25)				
III		33 (75)				
IGCCC risk group for metastatic disease, 33 patients, <i>n</i> (%)						
Good		8 (24.24)				
Intermediate		18 (54.54)				
Poor		7 (21.21)				
Chemotherapy regimen delivered in primary testicular tumor and response to chemotherapy according to the RECIST 1.1 criteria						
Type of Chemotherapy	Number of patients, <i>n</i> (%)	Median number of cycle (range)				
First-line chemotherapy	62 (84.94)					
BEP	44 (70.96)	4 (3–7)				
BEP+ EP	14 (22.58)	5 (4–6)				
EP	4 (6.45)	4 (4–6)				
Salvage chemotherapy	11 (15.06)					
VelP	6 (0.08)	6 (6–8)				
TIP	2 (0.03)	NA (6–8)				
VelP + TIP	1 (1.5)	6				
Gemcitabine + oxaliplatin	2 (0.03)	NA (5–9)				
Best response to last chemotherapy						
Type of chemotherapy	Radiological response according to RECIST 1.1, <i>n</i> (%)			STM, <i>n</i> (%)		
	Partial response	Stable disease	Progressive disease	<i>n</i>	Positive	Negative
After first-line chemotherapy ( <i>n</i> =55)	24 (63)	22 (40)	9 (16)	<i>n</i> =61	15 (24)	46 (75)
After salvage chemotherapy ( <i>n</i> =11)	6 (54)	3 (27)	2 (18)	<i>n</i> =10	4 (40)	6 (60)

STM=Serum tumor markers, AFP=Alpha fetoprotein, β hCG=Beta-human chorionic gonadotropin, LDH=Lactate dehydrogenase, MGCT=Mixed Germ cell tumor, UICC=International Union Against Cancer, IGCCC=International Germ Cell Consensus Classification, EP=Etoposide, cisplatin, BEP=Bleomycin, etoposide, cisplatin, VeIP=Vinblastin, ifosfamide, cisplatin, TIP=Paclitaxel, ifosfamide, cisplatin, NA=Not applicable, RECIST=Response Evaluation Criteria in Solid Tumors version 1.1, UDT=Undescended testis, SD=Standard deviation

### Histopathology

Fibrosis or necrosis was observed in 29 (39.7%) patients, teratoma in 33 (45.2%) patients, and residual viable tumors in 11 (15.1%) patients [Table 2].

### Metastasectomies

All seven metastasectomies were done as a separate procedure after the HPE of the pcRPLND was reported. All cases were following Standard pcRPLND. These surgeries were executed at about 4–6 weeks after pcRPLND. The concordance between RPLND and metastasectomy was 71.4% [Table 2 shows locations of metastasectomies and concordance with pre-chemotherapy, and pcRPLND HPEs].

### Follow-up and survival

The median follow-up was 26.72 months (IQR 13.25–47.84). The 2-year RFS was 93% (95% confidence interval [CI] – 83%–97%) and the OS rate was 90% (95% CI 80%–95%). There were no events in the good and intermediate groups [Figure 2 shows the Kaplan–Meier survival curves]. None of the patients who were diagnosed to have GTS had a recurrence on follow-up.

### DISCUSSION

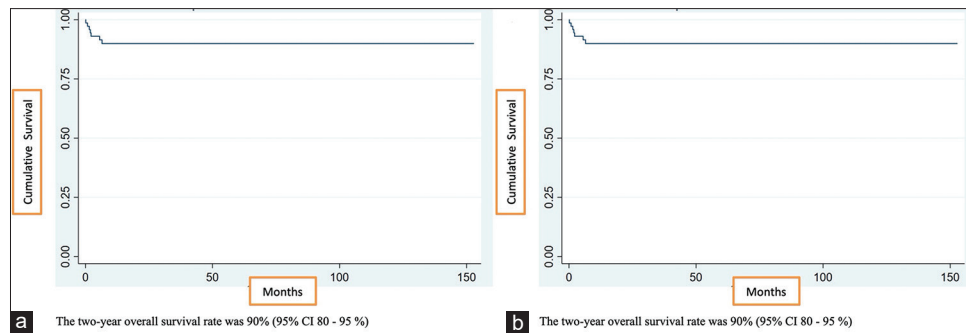
Three-fourths of patients had metastatic NSGCT at presentation. Of which, 24.24%, 54.54%, and 21.21% belonged to the good, intermediate, and poor IGCCC

**Table 2: Retroperitoneal lymph node dissection operative details, including postoperative complications according to Clavien-Dindo classification and metastasectomies and concordance with pre- and postchemotherapy retroperitoneal lymph node dissection histopathological examinations**

Characteristics	Standard pcRPLND (n=62)	Salvage pcRPLND (n=7)	Desperation pcRPLND (n=4)	Total cohort (n=73)
Mean operative time in hours (SD)	6.2 (2.59)	6 (1.67)	3.6 (0.57)	6.1 (2.46)
Median hospital stay in days, (IQR)	8 (6-10)	8 (7-10)	9 (9-10)	8 (7-10)
Adjunctive procedures, n (%)				
Nephrectomy	4 (6.4)	0	1 (25)	5 (6.84)
Duodenal primary repair	2 (3.2)	0	2 (50)	4 (5.5)
Renal artery anastomosis	1 (1.6)	0	0	1 (1.4)
Aortic grating	0	1 (14)	0	1 (1.4)
Uretero-ureterostomy	1 (1.6)	0	0	1 (1.4)
Cholecystectomy and segmental hepatectomy	1 (1.6)	0	0	1 (1.4)
Small bowel resection and anastomosis	0	0	1 (25)	1 (1.4)
Histopathological examination of RPLND, n (%)				
Teratoma, 3	26 (41)	5 (71)	2 (50)	33 (45.2)
Necrosis and fibrosis, 1	25 (40)	2 (28)	2 (50)	29 (39.7)
Viable tumor, 2	11 (17)	0	0	11 (15.1)
<b>30-day Clavien-Dindo grade, n (%)</b>				
I	15	1	1	17 (23.30)
Superficial wound infection				
Transient ileus				
II	7	0	1	8 (11.0)
Blood transfusion				
TPN				
Inotropic used				
IIIb	1	0	0	1 (1.4)
Re-exploration under GA				
IVa	5	2	0	7 (9.60)
Dialysis				
Pulmonary embolism				
NIV requiring intensive care monitoring				
AKI				
V	1	1	3	5 (6.8)
Death				
<b>Causes of 30-day postoperative mortality</b>				
Cause of death	Classification and details of surgery		HPE of PCRD	
Probable massive pulmonary embolism	Desperation RPLND, right ureteric catheterization, duodenal injury repair, and ileal resection and anastomosis		Mixed GCT with immature teratoma	
Pan-resistant pseudomonas pneumonia and septic shock	Desperation RPLND for primary RP GCT and right nephrectomy Comorbidities - chronic kidney disease		Necrosis	
Intestinal obstruction and associated metabolic acidosis - this patient had multiple episodes of intractable vomiting and nonresolving intestinal obstruction (documentation to justify why the patient was not posted sooner for re-exploratory surgery was not available)	Desperation RPLND and excision of metastatic duodenal polyp (3 <sup>rd</sup> part)		PCRd - Mixed GCT Duodenum - GCT with yolk sac component	
Hemorrhage into intracranial metastases	Salvage RPLND Died within 30 days after surgery (uneventful postoperative period)		Necrosis	
Intractable seizures due to intracranial metastases	Standard RPLND Died within 30 days after surgery (uneventful postoperative period)		Necrosis	
Metastasectomy (all were after standard RPLND)	Prechemotherapy HPE	pcRPLND HPE	Metastasectomy HPE	
Posterior mediastinal and supraclavicular LN excision	Yolk sac	Teratoma	Teratoma	
Wedge resection of lung nodule and posterior mediastinal LN excision	Yolk sac	Viable tumor	Teratoma	
	MGCT	Teratoma	Teratoma	
Wedge resection of lung and mediastinal and neck LN excision	MGCT	Teratoma	Teratoma	
Posterior mediastinum and supraclavicular LN excision	Teratoma	Teratoma	Teratoma	
Supraclavicular LN excision	MGCT	Teratoma	Necrosis	
Cholecystectomy and segmental hepatectomy	MGCT	Necrosis	Necrosis	

RP=Retroperitoneal, RPLND=RP lymph node dissection, TPN=Total parenteral nutrition, GA=General anesthesia, NIV=Noninvasive ventilation, AKI=Acute kidney injury, GCT=Germ cell tumor, HPE=Histopathological examination, PCRd=Postchemotherapy residual disease, pcRPLND=Postchemotherapy RPLND, SD=Standard deviation, IQR=Interquartile range, MGCT=Mixed Germ Cell tumour, LN=Lymph node





**Figure 2:** Kaplan–Meier survival curves (a) overall survival, (b) recurrence-free survival

risk groups. This observation was different from that observed in the cohort on which the IGCCCG framed the IGCCCG risk criteria, wherein 56%, 28%, and 16% distribution was seen, respectively.<sup>[19]</sup> In a similar clinical set-up as ours, Malik *et al.* observed a distribution of 30%, 20%, and 50%, respectively.<sup>[3]</sup> A higher percentage of the intermediate and poor risk categories may be because our institution is a referral center. IGCCCG risk categories are not predictive of residual tumor at the time of pcRPLND, with all three categories having a similar incidence of residual tumor at ~16%; however, they are predictive of recurrence and survival.<sup>[20]</sup> Past series have reported ~50% necrosis or fibrosis, 35% teratoma, and 15% viable tumor on HPE of PCRD, as did Singh *et al.*<sup>[5,21]</sup> We observed a similar percentage of viable tumors, i.e., 15%. However, Nagaraj *et al.* and Malik *et al.* both reported 10% and 7% of viable tumors, respectively, the latter attributing this reduction to advancement in multimodality treatment.<sup>[3,4]</sup> Another possible hypothesis for the higher observation of viable tumors is that we included patients who received chemotherapy elsewhere and their protocols may not be standard. Furthermore, Nagaraj *et al.* and Singh *et al.* included seminoma in their cohort, and chemotherapy details were not available.<sup>[4,5]</sup> Therefore, useful comparative deductions cannot be made.

Malik *et al.* observed similar findings with a 75% size reduction.<sup>[3]</sup> In our study, at least an 85% size reduction in the size of retroperitoneal lymph nodal mass predicted necrosis. However, similar experiences have not been reported consistently. Hence, avoiding pcRPLND just based on this single criterion after chemotherapy is not recommended.<sup>[22,23]</sup>

Beck *et al.*, from the Indiana University database, demonstrated that 48% of the patients without teratoma in the orchidectomy specimen had teratoma in the pcRPLND.<sup>[24]</sup> In this study, 17% of patients without teratoma in the original specimen had teratoma in the pcRPLND specimen. Hence, the absence of teratoma in the orchidectomy specimen does not rule out the probability of the same in the retroperitoneum. Furthermore, teratoma does not respond to chemotherapy and may develop GTS

or malignant transformation and, hence, requires surgical resection.

Vascular surgeries (~5%–15%) and nephrectomy (5%–19%) were the most common additional procedures in patients who had pcRPLND in other studies.<sup>[12–14,25]</sup> Adjuvant procedures were necessary for 13%–33% of patients in the Western literature, while our cohort observed a 15.6% need.<sup>[12,25,26]</sup> In our study, the most common adjunct procedures were nephrectomy (6.8%) and duodenal repair (4%). We had only two instances of vascular repair. Despite three-fourths of our cohort being stage 3, there were fewer instances of vascular repair requiring grafting and extirpative surgeries as adjunct procedures when compared to other centers.<sup>[12]</sup> Malik *et al.* and Nagaraj *et al.* did not put forward their data on adjunctive procedures.<sup>[3,4]</sup> Singh *et al.* had observed a similar frequency for adjunctive procedures.<sup>[5]</sup>

We observed a Clavien-Dindo  $\geq 3$  grade complication rate of 17%. Singh *et al.* observed a rate of 8.5% and Vasudeo *et al.* observed a rate of 13% after robotic-assisted RPLND.<sup>[5,6]</sup> The higher rate of complications may be due to the extent of disease burden persisting at the time of surgery.

Metastasectomy is necessary when significant extraretroperitoneal PCRD exists, especially when teratoma and viable tumors are found in the pcRPLND. Our study showed a 71.4% concordance rate between RPLND and metastasectomy and 50% between orchidectomy and metastasectomy. Steyerberg *et al.*, in multicenter studies, reported a high concordance of necrosis between pcRPLND with nonretroperitoneal PCRD of up to 89%.<sup>[27,28]</sup> Reliable indicators that can avoid metastasectomy even when necrosis is present in the retroperitoneum are still not considered standard since discordance of up to ~30% has been reported in various studies.<sup>[29–31]</sup>

The median follow-up was 26.72 months (IQR 13.25–47.84). The 2-year RFS was 93% (95% CI – 83%–97%) and the OS rate was 90% (95% CI 80%–95%). Only one other tertiary-care center in our country has published their survival outcomes. Singh *et al.* observed from their cohort of 35 patients (including seminoma [4%]) that at a median

follow-up of 33 months, 7 patients had recurrences and the estimated survival at 5 years was 83.7%.<sup>[5]</sup> Since we are a referral center, we have patients who travel long distances for treatment. Very few centers in India have the medical resources to support the execution of pcRPLND. In our literature review, we identified only six other institutes in the country that published their experience in India.<sup>[2-6,32]</sup> Of these, only one study projected an estimated RFS at 5 years after a 33-month median follow-up period after open pcRPLND.<sup>[5]</sup> Another study published their experience with 37 patients after robot-assisted pcRPLND with a median follow-up of 41 months. In their follow-up period, they found that only one patient had a recurrence.<sup>[6]</sup> These short median follow-up periods, as experienced by other tertiary care centers in our country, support our hypothesis that most patients do not follow up at their primary surgical treatment center and presumably continue surveillance closer to home. Experiences in India are tabulated in Table 3. The 5-year RFS was 90% (95% CI 89%–91%), 78% (95% CI 76%–80%), and 54% (95% CI 52%–56%) and OS was 96% (95% CI 95%–96%), 89% (95% CI 88%–91%), and 67% (95% CI 65%–69%) in the good, intermediate, and poor risk categories, respectively, according to the results from the IGCCCG updated consortium on following up

9,728 men with metastatic NSGCT.<sup>[33]</sup> We did not compute survival data for various subgroups as stated by the IGCCCG because our cohort is relatively smaller. However, the survival pattern of this cohort is encouraging even though statistical comparisons cannot be made.

The strengths that we can identify are that these are observations derived from a real-world dataset from India, which has given us information regarding survival, adjunctive procedures, and postoperative complications, which have not been documented by others in India consistently.

This study was retrospective and hence suffers the pitfalls associated with such. We were not able to collect data on the following parameters – blood loss, blood transfusion necessity, bowel recovery, or duration of intensive care due to inconsistent documentation. This information would have been useful to more accurately describe the extent of morbidity associated with pcRPLND. The department’s protocol is to follow a bilateral infra-hilar standard template. However, there have been on-occasion deviations from protocol and insufficient documentation, especially in the earlier decade. This information would have been useful

**Table 3: Comparison of outcomes between Indian publications on postchemotherapy retroperitoneal lymph node dissection**

Comparator parameters	Author, year of publication					
	Singh, 2016 <sup>[5]</sup>	Malik, 2020 <sup>[3]</sup>	Biswas, 2020 <sup>[2]</sup>	Nair, 2020 <sup>[32]</sup>	Vasudeo, 2023 <sup>[6]</sup>	Our cohort
Period of study	2003–2012	1994–2015	2011–2019	2006–2016	2012–2021	2003–2022
Cohort size	35 (29 – standard, 6 – salvage)	72	11	14	37	73 (62 – standard, 7 – salvage, 4 – desperation)
Inclusion criteria	pcRPLND in testicular GCT*	pcRPLND in NSGCT	NSGCT - all stages outcomes	NSGCT - all stages outcomes	Robot assisted-pcRPLND - for testicular GCT*	pcRPLND in NSGCT
Median follow-up (months)	33 (R-9–60)	NA	26.6 (R-2.2–100)	81 (entire cohort)	41 (IQR 14–64)	26.72 (IQR 13.25–47.84)
Stage III (%)	28.5	55.5	49	48.7	NA	75
Intermediate risk IGCCCG group	28.5	20	19	27.9	14	54.54
Poor risk IGCCCG group	31.4	50	49	20.4	5	21.21
HPE of pcRPLND, n (%)						
Fibrosis or necrosis	17 (48.5)	33 (45.83)	2 (18)	5 (35)	24 (65)	29 (39.7)
Mature teratoma	12 (34.2)	32 (44.44)	5 (45)	5 (35)	11 (30)	33 (45.2)
Viable tumor	6 (17.1)	7 (9.7)	6 (54)	4 (28)	2 (5)	11 (15.1)
Adjunct procedures	14 (40) required 15 adjunctive procedures	NA	NA	NA	NA	11 (15.06) required 14 adjunctive procedures
30-day postoperative complication rate ≥ Clavien–Dindo 3	3 (8.5) <sup>†</sup>	NA	NA	NA	5 (13.5)	13 (17.8)
30-day mortality	0 <sup>‡</sup>	NA	‡	‡	No postoperative mortality	5 (6.8) (30-day)
RFS 5 years (%) (95% CI)	83.7	NA	‡	‡	Only one recurrence was reported in the follow-up period	93 (83–97)
5 years OS (%), (95% CI)	NA	NA	‡	‡	NA	90 (80–95)

\*Testicular GCT - including both seminoma and NSGCT, †Duration within which mortality and morbidity took place is not clear, ‡pcRPLND subgroup analysis data not available. GCT=Germ cell tumor, HPE=Histopathological examination, pcRPLND=Postchemotherapy retroperitoneal lymph node dissection, RFS=Recurrence-free survival, OS=Overall survival, NA=Data not available, CI=Confidence interval, IQR=Interquartile range, IGCCCG=International Germ Cell Consensus Classification, NSGCT=Nonseminomatous GCT

to create associations between the limit of surgery and associated morbidity, recurrence, and survival.

Information is still sparse concerning the role of primary RPLND, nerve-sparing RPLND, modified templates of RPLND, and minimally invasive techniques (laparoscopic and robot-assisted laparoscopic approaches) in India. These are areas in which future research will help in standardizing their roles in routine management protocols subsequently.

## CONCLUSION

This is the largest series of pCRPLND for NSGCT in India to our knowledge. Although most of our cohort belonged to stage III, an RFS and OS rates of >90% at 2 years was observed. We believe that management of PCRDL in NSGCT is contingent on the availability of multidisciplinary expertise and is therefore best done at tertiary-care referral centers.

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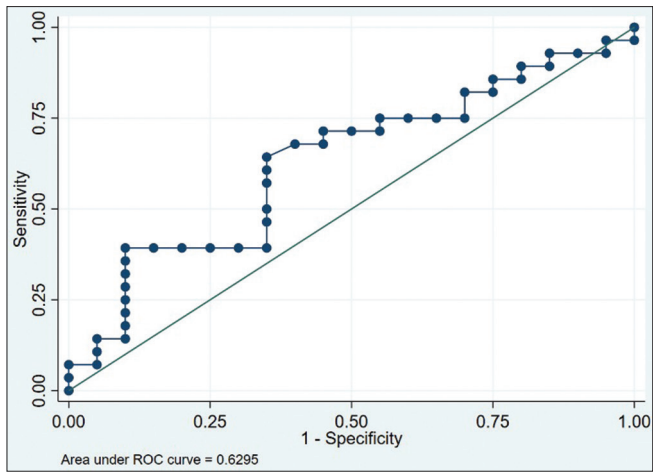
## REFERENCES

1. Cancer Today. Available from: <https://gco.iarc.fr/today/home>. [Last accessed on 2024 Jan 22].
2. Biswas B, Dabkara D, Ganguly S, Ghosh J, Gupta S, Sen S, *et al.* Outcome of testicular non-seminomatous germ cell tumours: Report from a tertiary cancer centre in Eastern India. *Ecancermedicallscience* 2021;15:1204.
3. Malik K, Raja A, Radhakrishnan V, Kathiresan N. A retrospective analysis of patients undergoing postchemotherapy retroperitoneal lymph node dissection and metastasectomy in advanced nonseminomatous germ cell tumors. *Indian J Urol* 2020;36:112-6.
4. Nagaraj RV, Rao BV, Yoganarsimha J, Fonseca D, Kodandapani S, Giridhar A, *et al.* Post-treatment residual clinicopathological outcomes in testicular germ cell tumours. *Indian J Surg Oncol* 2022;13:505-10.
5. Singh P, Yadav S, Mahapatra S, Seth A. Outcomes following retroperitoneal lymph node dissection in postchemotherapy residual masses in advanced testicular germ cell tumors. *Indian J Urol* 2016;32:40-4.
6. Vasudeo V, Khanna A, Pratihari SK, Jaipuria J, Chakraborty A, Rawal SK, *et al.* Robot-assisted retroperitoneal lymph node dissection for post-chemotherapy residual mass in testicular cancer: Long-term experience from a tertiary care centre. *J Minim Access Surg* 2023;19:288-95.
7. Donohue JP, Leibovitch I, Foster RS, Baniel J, Tognoni P. Integration of surgery and systemic therapy: Results and principles of integration. *Semin Urol Oncol* 1998;16:65-71.
8. Sheinfeld J. The role of adjunctive postchemotherapy surgery for nonseminomatous germ-cell tumors: Current concepts and controversies. *Semin Urol Oncol* 2002;20:262-71.
9. Hendry WF, Norman AR, Dearnaley DP, Fisher C, Nicholls J, Huddart RA, *et al.* Metastatic nonseminomatous germ cell tumors of the testis: Results of elective and salvage surgery for patients with residual retroperitoneal masses. *Cancer* 2002;94:1668-76.
10. Hartmann JT, Candelaria M, Kuczyk MA, Schmoll HJ, Bokemeyer C. Comparison of histological results from the resection of residual masses at different sites after chemotherapy for metastatic non-seminomatous germ cell tumours. *Eur J Cancer* 1997;33:843-7.
11. Steyerberg EW, Keizer HJ, Habbema JD. Prediction models for the histology of residual masses after chemotherapy for metastatic testicular cancer. ReHiT study group. *Int J Cancer* 1999;83:856-9.
12. Djaladat H, Nichols C, Daneshmand S. Adjuvant surgery in testicular cancer patients undergoing postchemotherapy retroperitoneal lymph node dissection. *Ann Surg Oncol* 2012;19:2388-93.
13. Stephenson AJ, Tal R, Sheinfeld J. Adjunctive nephrectomy at post-chemotherapy retroperitoneal lymph node dissection for nonseminomatous germ cell testicular cancer. *J Urol* 2006;176:1996-9.
14. Nash PA, Leibovitch I, Foster RS, Bihle R, Rowland RG, Donohue JP. En bloc nephrectomy in patients undergoing post-chemotherapy retroperitoneal lymph node dissection for nonseminomatous testis cancer: Indications, implications and outcomes. *J Urol* 1998;159:707-10.
15. Mead GM, Stenning SP. The international germ cell consensus classification: A new prognostic factor-based staging classification for metastatic germ cell tumours. *Clin Oncol (R Coll Radiol)* 1997;9:207-9.
16. RECIST 1.1. Available from: <https://recist.eortc.org/recist-1-1-2/>. [Last accessed on 2023 Sep 08].
17. Clavien PA, Barkun J, de Oliveira ML, Vauthey JN, Dindo D, Schulick RD, *et al.* The Clavien-Dindo classification of surgical complications: Five-year experience. *Ann Surg* 2009;250:187-96.
18. Kaplan EL, Meier P. Nonparametric estimation from incomplete observations. *J Am Stat Assoc* 1958;53:457-81.
19. International germ cell consensus classification: A prognostic factor-based staging system for metastatic germ cell cancers. International Germ Cell Cancer Collaborative Group. *J Clin Oncol* 1997;15:594-603.
20. Spiess PE, Brown GA, Pisters LL, Liu P, Tu SM, Evans JG, *et al.* Viable malignant germ cell tumor in the postchemotherapy retroperitoneal lymph node dissection specimen: Can it be predicted using clinical parameters? *Cancer* 2006;107:1503-10.
21. Sim HG, Lange PH, Lin DW. Role of post-chemotherapy surgery in germ cell tumors. *Urol Clin North Am* 2007;34:199-217.
22. Carver BS, Shayegan B, Serio A, Motzer RJ, Bosl GJ, Sheinfeld J. Long-term clinical outcome after postchemotherapy retroperitoneal lymph node dissection in men with residual teratoma. *J Clin Oncol* 2007;25:1033-7.
23. Lavery HJ, Bahnsen RR, Sharp DS, Pohar KS. Management of the residual post-chemotherapy retroperitoneal mass in germ cell tumors. *Ther Adv Urol* 2009;1:199-207.
24. Beck SD, Foster RS, Bihle R, Ulbright T, Koch MO, Wahle GR, *et al.* Teratoma in the orchiectomy specimen and volume of metastasis are predictors of retroperitoneal teratoma in post-chemotherapy nonseminomatous testis cancer. *J Urol* 2002;168:1402-4.
25. Heidenreich A, Haidl F, Paffenholz P, Pape C, Neumann U, Pfister D. Surgical management of complex residual masses following systemic chemotherapy for metastatic testicular germ cell tumours. *Ann Oncol* 2017;28:362-7.
26. Blok JM, Meijer RP, van der Poel HG, Bex A, van Vooren J, van Urk JJ, *et al.* Additional surgical procedures and perioperative morbidity in post-chemotherapy retroperitoneal lymph node dissection for metastatic testicular cancer in two intermediate volume hospitals. *World J Urol* 2021;39:839-46.
27. Steyerberg EW, Keizer HJ, Fosså SD, Sleijfer DT, Toner GC, Schraffordt Koops H, *et al.* Prediction of residual retroperitoneal mass histology after chemotherapy for metastatic nonseminomatous germ cell tumor: Multivariate analysis of individual patient data from six study groups. *J Clin Oncol* 1995;13:1177-87.
28. Steyerberg EW, Keizer HJ, Messermer JE, Toner GC, Schraffordt Koops H, Fosså SD, *et al.* Residual pulmonary masses after chemotherapy for metastatic nonseminomatous germ cell tumor. Prediction of histology. ReHiT Study Group. *Cancer* 1997;79:345-55.
29. Tiffany P, Morse MJ, Bosl G, Vaughan ED Jr., Sogani PC, Herr HW, *et al.* Sequential excision of residual thoracic and retroperitoneal



- masses after chemotherapy for stage III germ cell tumors. *Cancer* 1986;57:978-83.
30. Tognoni PG, Foster RS, McGraw P, Heilman D, Bihrlé R, Rowland RG, *et al.* Combined post-chemotherapy retroperitoneal lymph node dissection and resection of chest tumor under the same anesthetic is appropriate based on morbidity and tumor pathology. *J Urol* 1998;159:1833-5.
31. Mandelbaum I, Yaw PB, Einhorn LH, Williams SD, Rowland RG, Donohue JP. The importance of one-stage median sternotomy and retroperitoneal node dissection in disseminated testicular cancer. *Ann Thorac Surg* 1983;36:524-8.
32. Nair LM, Krishna KM, Kumar A, Mathews S, Joseph J, James FV. Prognostic factors and outcomes of nonseminomatous germ cell tumours of testis-experience from a tertiary cancer centre in India. *Ecancermedalscience* 2020;14:1145.
33. Gillissen S, Sauvé N, Collette L, Daugaard G, de Wit R, Albany C, *et al.* Predicting outcomes in men with metastatic nonseminomatous germ cell tumors (NSGCT): Results from the IGCCCG update consortium. *J Clin Oncol* 2021;39:1563-74.

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**Supplementary Appendix Figure 1:** Receiver operating curve - prediction of necrosis from a change in the size of retroperitoneal mass after chemotherapy