Restricted access and advanced disease in post-pandemic testicular cancer

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ABSTRACT

Introduction: Urologists observed reduced cancer consultations and surgeries during the SARS-CoV-2 pandemic, raising concern about treatment delays. Testicular cancer serves as a particularly sensitive marker of this phenomenon, as the clinical stage of testicular cancer at presentation is predictive of cancer-specific survival. We aimed to investigate whether COVID-related restrictions to primary care access resulted in increased incidence of metastatic germ cell testis cancer.

Methods: A retrospective chart review was conducted on all cases of testicular cancer managed surgically at our center from March 1, 2018, to February 28, 2023. Patients were categorized into temporal cohorts, representing before, during, and following the implementation of COVID-19 public health restrictions in the province of Newfoundland and Labrador.

KEY MESSAGES

- A retrospective chart review was conducted on all cases of testicular cancer managed surgically at our center from March 1, 2018, to February 28, 2023, and data was compared in three cohorts: before, during, and following COVID-19 public health restrictions.
- Clinical stage 3 disease remained stable before and during the pandemic at. Post-pandemic, there was an increase.
- Access to a family doctor and surgical wait times remained stable throughout the pandemic.
- Our study failed to identify a statistically significant rise in the incidence of metastatic disease after the lifting of pandemic restrictions but did highlight a relative increase in clinic stage III disease.

Results: Forty-one cases of testicular germ cell tumors were identified during the study period. The mean age at diagnosis was 40.8 years (standard deviation ±13.7). Demographics did not vary across the cohorts. Clinical stage 3 disease remained stable before and during the pandemic at 10.5% and 9.1% of cases, respectively. In the post-pandemic period, there was an increase to 27.3% (p=0.617). Surgical wait times remained stable across the pandemic (p=0.151).
Conclusions: There was a 16.8% rise in clinical stage III disease from the pre-pandemic to post-pandemic period. Our study failed to identify a statistically significant increase in metastatic testis cancer incidence upon lifting of pandemic restrictions. Further study is necessary to confirm suspicions that pandemic restrictions contributed to increased incidence of metastatic testis cancer.

INTRODUCTION

The SARS-CoV-2 virus brought unprecedented healthcare disruptions and placed an enormous strain on hospitals. This crisis forced a re-evaluation of conventional practices, resulting in restricted access to all manners of healthcare.[1,2] Nonurgent medical care, and in some cases, cancer care, was postponed.[3]

Urologists observed reduced cancer consultations and surgeries during this period, raising concern about treatment delays.[1,4,5] Testicular cancer serves as a particularly sensitive marker of this phenomenon as the clinical stage of testicular cancer at presentation is predictive of cancer-specific survival.[6–9] Clinical studies have consistently shown that patients with early-stage testicular cancer can expect a cure rate approaching 100%, while those in advanced stages have a cure rate ranging from 70% to 80%.[6,7,10] Lower cure rates may suggest insufficiencies within the healthcare system in identifying these malignancies.

Most men present with a palpable mass within the testicle, which may or may not be accompanied by pain. Appropriate work-up includes a scrotal examination, ultrasound, measurement of serum tumor markers, and a staging CT scan. If these investigations suggest possible malignancy, the patient is offered a radical orchiectomy.[11–13] Current guidelines delineate that suspected cases of testicular cancer are to be seen by a urologist within 2 weeks of initial presentation.[14]

We aimed to investigate whether COVID-related restrictions to primary care access resulted in an increased incidence of metastatic germ cell testis cancer following the pandemic restrictions. We performed a single-centre analysis of testicular germ cell tumours in Newfoundland and Labrador (NL), Canada assessing incidence and pathology of disease before, during, and after public health restrictions.

METHODS

Ethics approval was obtained from the Provincial Health Research Ethics Board at Memorial University in St. John's, NL, Canada. A retrospective chart review was conducted on all cases of testicular cancer managed surgically at our centre from March 1, 2018, to February 28, 2023. Patients who had undergone radical orchiectomy were identified using operating room codes. Pathology reports of each case were investigated to determine eligibility for this study, with non-malignant causes of orchiectomy being excluded. Stage of disease at presentation was according to the Canadian Urological Association (CUA) guidelines.[11] Patients were categorized into temporal cohorts, representing before, during, and following the implementation of COVID-19 public health restrictions in the province of NL. The cohorts were defined as the following:

- Pre-pandemic: March 1, 2018 – March 31, 2020 (24 months)
- Pandemic: April 1, 2020 – February 28, 2022 (23 months)
- Post-pandemic: March 1, 2022 – February 28, 2023 (12 months)

The time interval between diagnosis and orchiectomy was recorded, and relevant data was extracted from pathology reports, diagnostic imaging reports, as well as chart reviews. Categorical data was compared using Pearson's Chi-square and Fischer's Exact test and continuous data was compared using independent sample t-test and Kruskal-Wallis test, with significance set at p=0.05. Statistical analyses were performed using SPSS version 27.0 (IBM Corporation, Armonk, NY). Continuous variables were reported as means and standard deviations or medians and interquartile ranges, while descriptive variables were presented as absolute counts and percentages.

RESULTS

We identified 79 individuals who underwent orchiectomy at our centre within the specified timeframe. Of these, 41 cases met the inclusion criteria of a diagnosis of testicular germ cell tumors that had been adequately followed (Figure 1).

Patient characteristics

The mean age at diagnosis was 40.8 years (SD ±13.7). A mean of 12.6 days (SD ±19.1) was found between diagnosis and surgery. The median body mass index (BMI) was 28.3 (IQR ±9.1). Obesity, defined as a BMI over 30, was present in 19 patients (46.3%). Lack of access to a family doctor was observed in 9 patients (22%). Current or former cigarette use was reported in 19 patients (46.3%), while cryptorchidism was identified in only 1 patient (2.4%). Data on the duration of symptoms was widely underreported.

Tumor characteristics

Clinical stage 3 disease remained stable before and during the pandemic at 10.5% and 9.1% of cases, respectively. In the post-pandemic period, there was an increase to 27.3% (p=0.617). This rise in stage III disease amounted to a relative 16.8% increase. The distribution of clinical stages demonstrates a stable incidence of stage 2 and 3 cases before and during the pandemic.

Following the pandemic, we noted a decline in stage I cases with a marked increase in stage II and III disease (Figure 2).

Case outcomes
Fifteen cases (36.6%) exhibited metastatic disease. In the pre-pandemic cohort, all cases (100%) of metastatic disease were limited to the retroperitoneum or mediastinum. One case (33.3%) of pulmonary metastasis was reported during the pandemic. Following the pandemic, metastases were identified within 3 cases (50%) involving spread beyond the retroperitoneum to pulmonary, mesenteric, or pelvic lymph nodes. Retroperitoneal lymph node dissection was required in one case before the pandemic, one case during, and two cases after the pandemic.

Surgical wait times
One case underwent neo-adjuvant chemotherapy prior to orchiectomy and was therefore excluded from the analysis of surgical wait times. Across the study, the mean duration from diagnosis to orchiectomy was 12.59 days (SD ±19.1). These wait times remained stable from the pre-pandemic to the post-pandemic period (p=0.151; Table 1 and Figure 3).

DISCUSSION
To date, only three studies have investigated the impact of the COVID-19 pandemic on testicular cancer outcomes. Oderda et al. conducted a study investigating 41 cases at an academic referral centre and compared their data based on the year of orchiectomy.[15] They concluded there were no significant differences in pathological features but remarked that the median time between diagnosis and surgery remained below the recommended two weeks.[15]

Yildiz et al. in Turkey investigated 65 patients with germ cell tumours.[16] They dichotomized their data before and after the first COVID-19 cases in their country and both study periods were equal at 19 months.[16] They found a significant increase in the duration of symptoms, and increase in time from diagnosis to surgery.[16] They observed the risk of occult metastasis to be 45.5% before the pandemic and 76.5% after the pandemic, where the risk of occult metastasis is based on a tumour diameter greater than 4 cm or invasion into the rete testis.[16]

The largest study, conducted in Alberta, Canada, examined 335 patients with germ cell tumours.[17] Their study divided participants by April 2020, the first month with all pandemic restrictions, and covered 15 months before this date and 14 months after.[17] In this study, 7.8% of patients diagnosed before the pandemic presented with stage III disease, which increased to 15.4% during the pandemic.[17] The pandemic initially led to a decline in cases, followed by a significant increase in stage III disease and a decrease in stage II disease.[17]

Our study is one of a few assessing testicular cancer staging at presentation during the COVID-19 pandemic. It is the first study to investigate before, during, and after the removal of public health restrictions. Our hypothesis was that patients' delay in seeking primary care during the pandemic would lead to increased metastatic disease at presentation. Our study did not

confirm the hypothesis, as we couldn't establish a statistically significant increase in metastatic testis cancer incidence.

There was a non-statistically significant trend for a 16.8% increase in clinic stage III disease from the pre-pandemic to the post-pandemic period. During the introduction of public health restrictions in 2020, the incidence of metastatic disease remained stable. However, after the restrictions were lifted, it reached an unprecedented level. The decline in case counts in 2020 is concerning, as it aligns with the period of most extensive public health restrictions.

The stability of the time interval from diagnosis to orchiectomy over the course of the pandemic ($p=0.151$) suggests that every effort was made to maintain the standard of care for testis cancer in NL for those cases that were referred to urology.

Recent statistics from the Newfoundland and Labrador Medical Association reveal that 26% of the province's population lacks a family doctor, consistent with the 22% of patients enrolled in our study.[18] Notably, this number remained stable throughout the pandemic. Patients without access to a family doctor had to seek care through the emergency department or walk in clinics. Further research is warranted to determine if these patients experienced delayed presentation and delayed referral to urology.

Limitations

This research has several limitations that necessitate consideration. Most notably, our sample size is small, limiting statistical power.

Secondly, the unequal length of timeframes for pre-pandemic, pandemic, and post-pandemic period presents a statistical challenge when interpreting the results. To address this disparity, further research should be directed towards longitudinally assessing patient outcomes after the pandemic-related public health restrictions were lifted.

The retrospective design of this study introduces selection bias, potential for inconsistent reporting, and missing variables, which may lead to data inaccuracies. Particularly, limitations were encountered in obtaining data relevant to the duration and character of initial symptoms due to the use of our centre-based electronic medical record system, which does not integrate with the records used by family doctors.

CONCLUSIONS

The clinical stage of testicular cancer at presentation is predictive of cancer specific survival. Urologists observed reduced cancer consultations and surgeries during the SARS-CoV-2 pandemic, raising concern of treatment delays. Our study failed to identify a statistically significant rise in the incidence of metastatic disease after the lifting of pandemic restrictions. However, it did highlight a descriptive relative 16.8% increase in clinic stage III disease from the pre-pandemic to the post-pandemic period. Access to a family doctor as well as surgical wait times remained stable. Further study is necessary to confirm suspicions that pandemic restrictions contributed to increased incidence of metastatic testis cancer.

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FIGURES AND TABLES

Figure 1.

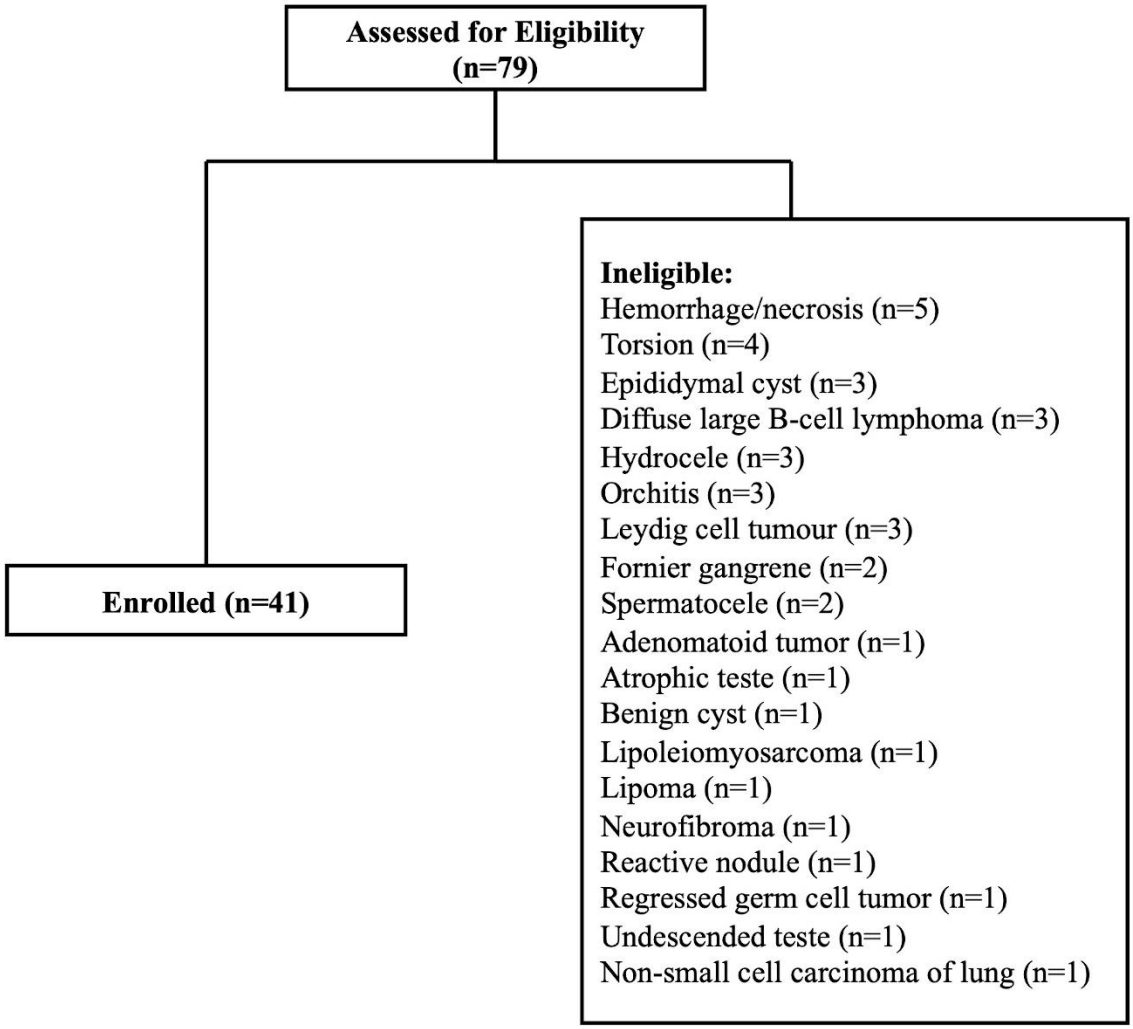

Figure 2.

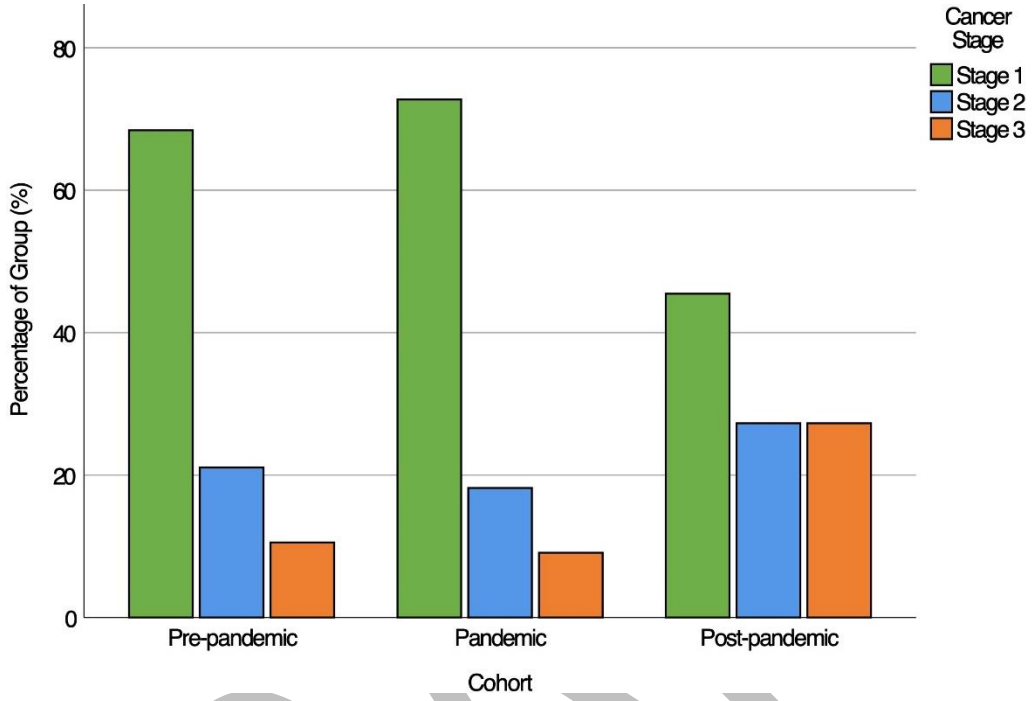

Figure 3.

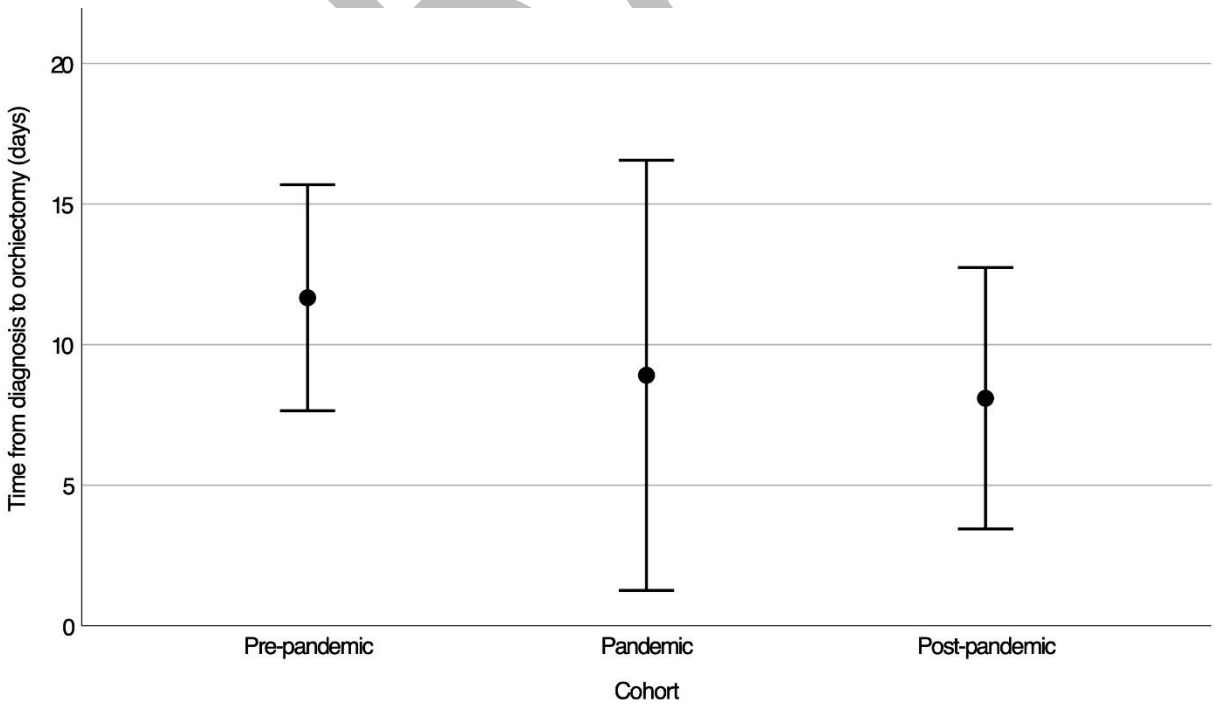

Table 1. Patient and presentation characteristics categorized by pandemic cohort				
	Pre-pandemic (n=19)	**Pandemic (n=11)**	**Post-pandemic (n=11)**	**p**
Age at diagnosis (years), mean ± SD	43.5±17.0	37.7±6.86	39.1±12.5	0.497
Time from diagnosis to surgery (days), mean ± SD	11.7±8.1	8.9±11.4	8.1±6.9	0.523
BMI (kg/m^2), median ± IQR	26.6±7.9	30.7±14.7	28.3±9.3	0.161
BMI classification				0.178
Normal	7 (36.8)	2 (18.2)	2 (18.2)	
Overweight	5 (26.3)	1 (9.1)	5 (45.5)	
Obese	7 (36.8)	8 (72.7)	4 (36.4)	
Family doctor				0.397
Yes	16 (84.2)	7 (63.6)	9 (81.8)	
No	3 (15.8)	4 (36.4)	2 (18.2)	
Cryptorchidism				0.678
No	14 (73.7)	9 (81.8)	7 (63.6)	
Yes	1 (5.3)	0 (0)	0 (0)	
Not mentioned	4 (21.1)	2 (18.2)	4 (36.4)	
Cigarette use				0.291
Never	9 (47.4)	5 (45.5)	7 (63.6)	
Formerly	2 (10.5)	1 (9.1)	3 (27.3)	
Currently	8 (42.1)	4 (36.4)	1 (9.1)	
Not mentioned	0 (0)	1 (9.1)	0 (0)	
Duration of symptoms				0.610
<1 month	3 (15.8)	3 (27.3)	3 (27.3)	
1–6 months	6 (31.6)	4 (36.4)	2 (18.2)	
6–12 months	2 (10.5)	2 (18.2)	0 (0)	
>12 months	1 (5.3)	0 (0)	0 (0)	
Not mentioned	7 (36.8)	2 (18.2)	6 (54.5)	

Format: Normally distributed data is represented as mean ± standard deviation, non-normally distributed data as median ± interquartile range, and nominal data as count (percentage). BMI: body mas index; IQR: interquartile range; SD: standard deviation.

Table 2. Tumor characteristics categorized by pandemic cohort				
	Pre-pandemic (n=19)	**Pandemic (n=11)**	**Post-pandemic (n=11)**	**p**
Afflicted testicle				0.836
Left	9 (47.4)	4 (36.4)	5 (45.5)	
Right	10 (52.6)	7 (63.6)	6 (54.5)	
Diagnostic method				0.296
Ultrasound	17 (89.5)	11 (100)	11 (100)	
Biopsy of retroperitoneal lymph node	2 (10.5)	0 (0)	0 (0)	
Pathology				0.515
Seminoma	5 (26.3)	3 (27.3)	1 (9.1)	
Non-seminoma	14 (73.7)	8 (72.7)	10 (90.9)	
T stage				0.491
pT1	12 (63.2)	5 (45.5)	5 (45.5)	
pT2	6 (31.6)	5 (45.5)	6 (54.5)	
pT3	0 (0)	1 (9.1)	0 (0)	
Not stated	1 (5.3)	0 (0)	0 (0)	
N stage				0.486
N0	13 (68.4)	8 (72.7)	5 (45.5)	
N1	3 (15.8)	0 (0)	1 (9.1)	
N2	2 (10.5)	1 (9.1)	2 (18.2)	
N3	1 (5.3)	2 (18.2)	3 (27.3)	
M stage				0.174
M0	17 (89.5)	8 (72.7)	8 (72.7)	
M1	0 (0)	2 (18.2)	0 (0)	
M1A	2 (10.5)	1 (9.1)	2 (18.2)	
M1B	0 (0)	0 (0)	1 (9.1)	
S stage				0.243
SX	0 (0)	2 (18.2)	1 (9.1)	

S0	15 (78.9)	6 (54.5)	5 (45.5)	
S1	3 (15.8)	3 (27.3)	3 (27.3)	
S2	1 (5.3)	0 (0)	2 (18.2)	
Cancer staging				0.425
Stage 1	0 (0)	2 (18.2)	1 (9.1)	
Stage 1A	9 (47.4)	3 (27.3)	3 (27.3)	
Stage 1B	3 (15.8)	3 (27.3)	1 (9.1)	
Stage 1S	1 (5.3)	0 (0)	0 (0)	
Stage 2A	3 (15.8)	0 (0)	1 (9.1)	
Stage 2B	1 (5.3)	0 (0)	0 (0)	
Stage 2C	0 (0)	2 (18.2)	2 (18.2)	
Stage 3A	2 (10.5)	1 (9.1)	1 (9.1)	
Stage 3B	0 (0)	0 (0)	1 (9.1)	
Stage 3C	0 (0)	0 (0)	1 (9.1)	

Format: Count (percentage).

Table 3. Outcome characteristics categorized by pandemic cohort

	Pre-pandemic (n=6)	**Pandemic (n=3)**	**Post-pandemic (n=6)**	**Total (n=15)**
Furthest spread of metastasis				
Retroperitoneum	4 (66.7)	2 (66.7)	3 (49.9)	9 (59.9)
Mediastinum	2 (33.3)	0 (0)	0 (0)	2 (13.3)
Pulmonary	0 (0)	1 (33.3)	1 (16.6)	2 (13.3)
Mesentery	0 (0)	0 (0)	1 (16.6)	1 (6.7)
Pelvic & mediastinum	0 (0)	0 (0)	1 (16.6)	1 (6.7)
Additional treatment				
Chemotherapy	5 (83.3)	1 (33.3)	4 (66.7)	10 (66.6)
Radiation	0 (0)	1 (33.3)	0 (0)	1 (6.7)
Post-chemotherapy RPLND	1 (16.6)	1 (33.3)	2 (33.3)	4 (26.7)

RPLND: retroperitoneal lymph node dissection.