Restricted access and advanced disease in post-pandemic testicular cancer

Mitchell Fagan[1], W.C. Ian Janes[1], Matthew Andrews[2], David R. Harvey[2], Geoff M. Warden[3], Michael K. Organ[2], Paul Johnston[2]

[1]Faculty of Medicine, Memorial University, St. John's, NL, Canada; [2]Department of Urology, Memorial University, St. John's, NL, Canada; [3]Discipline of Anesthesia, Memorial University, St. John's, NL, Canada

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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.

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 3 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 workup 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 two weeks of initial presentation.[14]

We aimed to investigate whether COVID-related restrictions to pri-

KEY MESSAGE

■ Our study failed to identify a statistically significant rise in the incidence of metastatic disease after the lifting of COVID-19 restrictions but did highlight a relative increase in clinical stage 3 disease.

mary care access resulted in an increased incidence of metastatic germ cell testis cancer following the pandemic restrictions. We performed a single-center analysis of testicular germ cell tumors 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. 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 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 to March 31, 2020 (24 months)
- Pandemic: April 1, 2020 to February 28, 2022 (23 months)
- Post-pandemic: March 1, 2022 to 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, and chart reviews. Categorical data was compared using Pearson's Chi-squared 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, U.S.). 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 center 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).

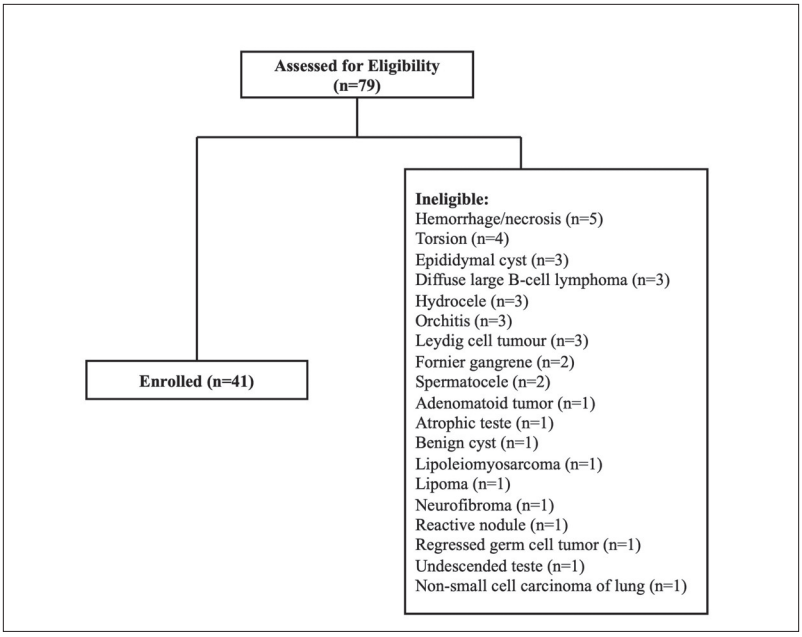

Figure 1. Flowchart sorting all orchiectomies from March 1, 2018, to February 28, 2023, at our center by the inclusion/exclusion criteria.

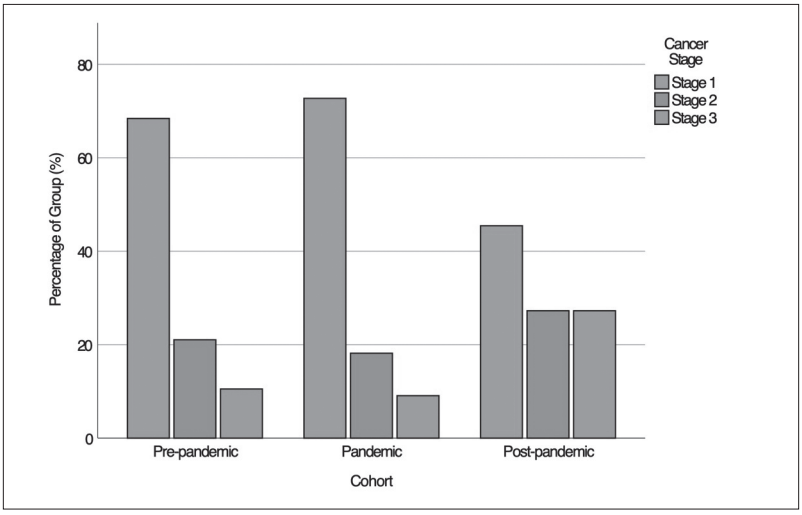

Figure 2. Distribution of clinical cancer stage across the study years.

Table 1. 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)	

Format: Count (percentage).

Table 1 (cont'd). Tumor characteristics categorized by pandemic cohort

	Pre-pandemic (n=19)	Pandemic (n=11)	Post-pandemic (n=11)	p
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).

Patient characteristics

The mean age at diagnosis was 40.8 years (standard deviation [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 (interquartile range [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 nine patients (22%). Current or former cigarette use was reported in 19 patients (46.3%), while cryptorchidism was identified in only one 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 3 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 1 cases with a marked increase in stage 2 and 3 disease (Figure 2, Table 1).

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 three 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 (Table 2).

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; Figure 3, Table 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 center 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 investigated 65 patients with germ cell tumors.[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 tumor 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 tumors.[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 3 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 3 disease and a decrease in stage 2 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 clinical stage 3 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;

Table 2. 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.

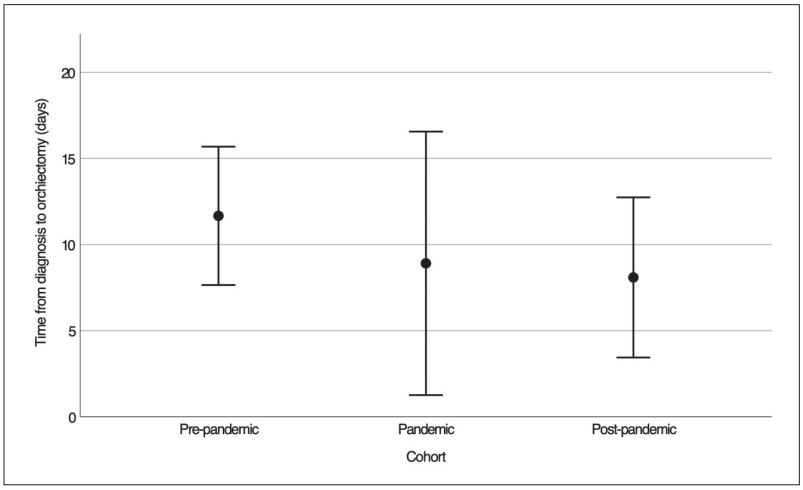

Figure 3. Time from diagnosis to orchiectomy across cohorts. Note: Bullet points are means and error bars are 95% confidence intervals.

Table 3. 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 mass index; IQR: interquartile range; SD: standard deviation.

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 whether 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 periods 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 center-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 clinical stage 3 disease from the pre-pandemic to the post-pandemic period. Access to a family doctor and surgical wait times remained stable. Further study is necessary to confirm suspicions that pandemic restrictions contributed to increased incidence of metastatic testis cancer.

COMPETING INTERESTS: The authors do not report any competing personal or financial interests related to this work.

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This paper has been peer reviewed.

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CORRESPONDENCE: Mitchell Fagan, Faculty of Medicine, Memorial University, St. John's, NL, Canada; mgfagan@mun.ca