## ORIGINAL RESEARCH

# Use of imaging for active surveillance in testicular cancer: Is real-world practice concordant with guidelines?



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#### Abstract

**Introduction:** Imaging is an integral component of active surveillance (AS) following orchiectomy for stage 1 non-seminoma (NSGCT) and seminoma germ cell tumors. In this population-based study, we describe use of imaging among patients with early-stage testicular cancer and evaluate whether they are concordant with guideline recommendations.

**Methods:** This is a population-based, retrospective cohort study to describe use of imaging among all patients with early-stage testicular cancer treated with AS in the Canadian province of Ontario. The Ontario Cancer Registry was linked to electronic records of treatment to identify use of chest and abdomen/pelvis imaging. Data from 2000–2010 were included, with followup for up to five years for patients with non-seminoma and 10 years for patients with seminoma. The key outcome of interest was the frequency of imaging at temporal milestones following orchiectomy. Compared to the most contemporaneous guidelines in Ontario, any discordant frequency of imaging was defined as underuse or overuse. Substantial under- or overuse was defined as >1 imaging test less/more than what was recommended during a 12-month period.

**Results**: The study population included 569 patients with NSGCT (median age 28) and 1107 with seminoma (median age 37). Among patients with NSGCT, adherence with body imaging was low in years 1–3 of surveillance (range 26–37%, predominantly underuse) and higher in years 4–5 (63–67%, predominantly overuse). Adherence with chest imaging was even lower (range 11–34% during years 1–5). Among patients with seminoma, adherence with abdominal and chest imaging was relatively stable and comparable throughout the 10-year followup period (range 23–47% abdomen and 28–47% chest). Multivariable analysis confirmed that underuse of imaging was more common in recent years. NSGCT histology was associated with underuse in years 1–2 but overuse in years 3–5. **Conclusions:** In routine clinical practice, patients with testicular cancer commonly receive imaging discordant to the protocol for AS, with a substantial proportion receiving both under- and overuse at various times during surveillance followup.

#### Introduction

Imaging is a critical component of active surveillance (AS) following orchiectomy, which is now the preferred treatment for patients with stage 1 non-seminoma (NSGCT) or seminoma germ cell tumors.<sup>1,2</sup> We previously reported that AS has been widely adopted in routine practice and is associated with excellent survival outcomes.3 Surveillance programs include regular imaging of the lungs and abdomen/ pelvis. These programs seek to balance the need for regular imaging to identify early, recurrent disease with the risks and harms of imaging overuse. Risks of overuse include discovery of incidental but clinically insignificant findings, radiation exposure, test-related anxiety and decreased quality of life, and financial costs to society. The risks of radiation exposure and subsequent secondary malignancy are relevant in this setting, given high expected long-term survival and young age at diagnosis.

Current guidelines for frequency of imaging during surveillance of stage 1 testicular cancer attempt to balance the competing risks of over- and underuse of imaging. A previous study has shown that the mean rates of compliance with chest X-ray and computed tomography (CT) scans for patients with stage I NSGCT treated in Canadian centers were 78% and 64%, respectively.<sup>4</sup> Population-based studies can provide insights into patterns of care and outcomes among patients treated in routine clinical practice.<sup>5,6</sup> In this

population-based study, we describe use of imaging among patients with early-stage testicular cancer and evaluate whether practice was concordant with contemporaneous guideline recommendations.

#### Methods

#### Study design and population

This is a population-based, retrospective cohort study to describe use of imaging among all patients with early-stage testicular cancer treated with AS in the Canadian province of Ontario. Ontario has a population of nearly 14 million people and a single-payer universal health insurance program. All incident cases age 16 years or above who underwent orchiectomy from 2000–2010 and were managed by AS were included. Patients were defined as being on surveillance if they had no chemotherapy, radiation, or retroperitoneal lymph node dissection within 90 days of orchiectomy. The study was approved by the Research Ethics Board of Queen's University, Kingston, ON, Canada. This study was designed, analyzed, and reported in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement.<sup>7</sup>

#### Data sources

The Ontario Cancer Registry (OCR) is a passive, populationbased cancer registry that captures diagnostic and demographic information for at least 98% of all incident cases of cancer in Ontario.<sup>8</sup> A variety of electronic administrative health databases were linked to the OCR, including Activity Level Reporting Data (ALR), a database of patient-level activity on radiation and systemic therapy services for cancer treatment; Canadian Institute of Health Information (CIHI), which contains information on hospitalizations and surgical procedures; and the Ontario Health Insurance Plan (OHIP), a database of physician claims for medical services provided. These services include laboratory tests, consults, surgeries, diagnostic tests, and therapeutic procedures.

We obtained surgical pathology reports for all orchiectomy procedures performed in Ontario from 2000–2010. The data were manually abstracted by trained personnel into a pre-piloted electronic database and linked using unique, encoded identifiers to several administrative health databases housed at the Institute for Clinical Evaluation Services. The CIHI database provides information about orchiectomy procedures. OHIP provincial physician billing records, along with electronic treatment records from regional cancer centers, were used to identify chemotherapy use. Use of imaging tests was identified from OHIP physician billing records. Data sets were linked with unique encoded identifiers and were analyzed at the Institute for Clinical Evaluation Services. Data from 2000–2010 were included, with followup for up to five years for patients with non-seminoma and 10 years for patients with seminoma, as per the practice guideline recommendations for duration of followup.

#### Measures and outcomes

The key outcome of interest was the frequency of imaging modalities at pre-identified temporal milestones following orchiectomy. Imaging use was compared to the guidelines from the Princess Margaret Cancer Centre (Toronto, ON), which were the most contemporaneous guidelines in Ontario at the time (1999–2010 for non-seminoma and 1995–2004 for seminoma) (Table 1). These guidelines are very similar to guidelines from the National Comprehensive Cancer Network (NCCN) and the European Society for Medical Oncology (ESMO) during the study period (no public links available for these past versions of the guidelines; authors can provide them upon request).

Underuse and overuse were defined for each year for CT abdomen/pelvis (CT AP) and chest imaging (CT chest or CXR) separately and were defined as imaging frequencies less than or more than the frequencies listed in Table 1. Year of imaging was measured from date of orchiectomy; imaging studies performed in the two months prior to orchiectomy were counted as year 1. Patients were excluded from the denominator for the ongoing and subsequent years in the event of death, further treatment, or incomplete availability of imaging data. A difference in the frequency by more than one was considered substantial overuse (>1 over) or substantial underuse (<1 under).

Table 1. Imaging frequency recommended by PrincessMargaret Hospital for patients with non-seminoma(guideline 1990-2010) and seminoma testicular cancer(guideline 1995-2004)

Year	Non-seminom	a annual tests	Seminoma annual tests		
	CT abdomen/ pelvis	CT chest or CXR	CT abdomen/ pelvis	CT chest or CXR	
1	4	7	4	2	
2	3	6	3	2	
3	0	3	3	1	
4	0	2	2	1	
5	0	1	2	1	
6	NA	NA	2	1	
7	NA	NA	2	1	
8	NA	NA	1	1	
9	NA	NA	1	1	
10	NA	NA	1	1	

Year is measured from discharge date of orchiectomy. Year 1 includes imaging done 2 months before orchiectomy. CT: computed tomography; CXR: chest X-ray; NA: not applicable.

#### Statistical analysis

We report the proportion of patients with over/underuse of imaging. Univariate and multivariate logistic regression was used to identify factors associated with over/underuse. Patients with over/underuse in any of the years of followup were classified as over/underuse "yes." Covariates considered in the model included year of orchiectomy, age group, region, tumor type (seminoma or non-seminoma), and high risk (defined as lymphovascular invasion positive for nonseminoma and tumor >4 cm or rete testes invasion for seminoma risk) or low risk for relapse. These analyses were done for years 1 and 2 and years 3-5 separately because the recommended frequencies of imaging drop substantially between first two years and rest of the years. For the regression analysis, we only included five years of followup for seminoma patients to be consistent with non-seminoma (i.e., years 6–10 were not considered) since both histologies were included in the model. Any patients who did not have complete followup were excluded from analysis for that year and subsequent years. Any cohort with five or fewer number of patients were not considered in the analyses. All the analyses were conducted in SAS version 9.4

#### Results

#### Study population

From 2000–2010, 3546 patients were diagnosed with testicular cancer in Ontario, including 3281 who had an orchiectomy identified (93%) (Supplementary Fig. 1; available at *cuaj.ca*). Pathology reports were available for 2821 (86%) of these cases. There were no significant differences in demographics, histology, or survival of those cases with (n=2821) and without (n=460)available orchiectomy pathology reports (Supplementary Fig. 2, Supplementary Table 1; available at *cuaj.ca*). One hundred (4%) cases were excluded, as the histology was not germ-cell tumor; 36 (1%) cases were excluded, as the date of pathology report and orchiectomy were not consistent; 35 (1%) cases were excluded, as they had other cancer-directed therapy before orchiectomy; and 974 patients were excluded who had radiation or systemic treatment within 90 days of orchiectomy. The study population included 1676 patients: 569 with NSGCT and 1107 with seminoma. Characteristics of the study population are shown in Table 2. Median age was 34 years (28 for NSGCT and 37 for seminoma). Twenty-six percent (149/569) of NSGCT and 35% (584/1107) of seminoma patients were classified as having high-risk disease.

Table 2. Characteristics of patients with non-seminoma andseminoma testicular cancer treated with orchiectomy andsurveillance in Ontario during 2000-2010

Characteristic	All patients	Non- seminoma	Seminoma	
	N=1676	n=569	n=1107	
		n (%)		
Age				
Mean/median (years)	36/34	31/28	38/37	
<20	84 (5.0%)	64 (11%)	20 (2%)	
20–29	466 (28%)	246 (43%)	220 (20%)	
30–39	570 (34%)	160 (28%)	410 (37%)	
40–49	385 (230%)	75 (13%)	310 (28%)	
50–59	122 (7%)	18 (3%)	104 (9%)	
60+	49 (3%)	6 (1%)	43 (4%)	
Primary histology				
Seminoma, NOS	1207 (72.0%)	100 (17.6%)	1107 (100.0%)	
Embryonal carcinoma, NOS	267 (15.9%)	267 (46.9%)	NA	
Teratoma, malignant, NOS	147 (8.8%)	147 (25.8%)	NA	
Yolk sac tumor	51 (3.0%)	51 (9.0%)	NA	
Choriocarcinoma, NOS	≤5	≤5	NA	
NA	≤5	≤5	NA	
Tumor size (cm)				
Mean/median	4/4	4/4	4/4	
≤4 cm	979 (58%)	326 (57%)	653 (59%)	
>4 cm	655 (40%)	233 (41%)	422 (38%)	
Unstated	42 (3%)	10 (2%)	32 (3%)	
Rete testis invasion				
Yes	440 (26%)	127 (22%)	313 (28%)	
No	677 (40%)	219 (38%)	458 (41%)	
Not stated	559 (33%)	223 (39%)	336 (30%)	
Lymphovascular invasion				
Yes	306 (18%)	149 (26%)	157 (14%)	
No	1,023 (61%)	298 (52%)	725 (65%)	
Not stated	347 (21%)	122 (21%)	225 (20%)	

#### specified.

#### Use of imaging

The pattern of under-imaging and over-imaging for both seminoma and non-seminoma cohort are provided in Fig. 1.

#### Non-seminoma

As shown in Table 3, among patients with NSGCT, adherence with body imaging was low in years 1–3 of surveillance (range 26–37%) and higher in years 4–5 (63-67%). In the earlier years, underuse of imaging was more common; this pattern shifted to overuse in later years. Substantial underuse of body imaging (i.e., >1 under-reported scan per year) was observed in 20% (87/432) and 36% (148/414) of patients in years 1 and

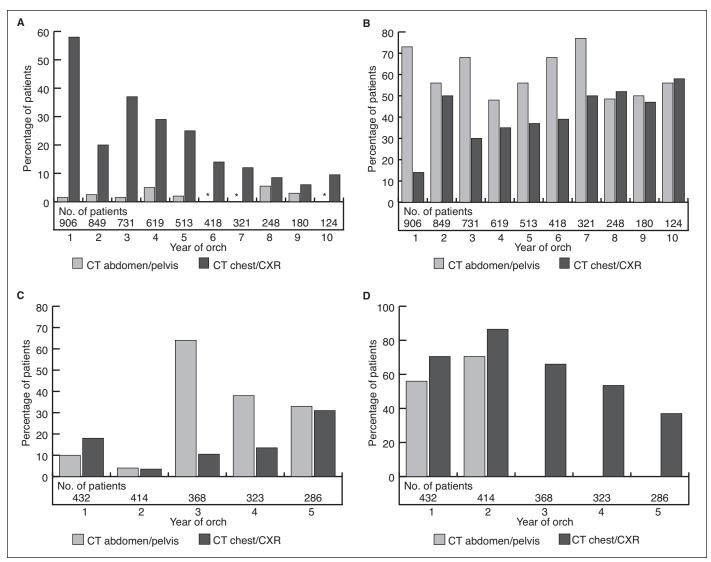


Fig. 1. Pattern of under-imaging and over-imaging for both seminoma and non-seminoma cohort. (A) Seminoma overuse. (B) Seminoma underuse. (C) Non-seminoma overuse. (D) Non-seminoma underuse. \*Suppressed owing to small cell count. CT: computed tomography; CXR: chest X-ray.

2, respectively. Substantial overuse of body imaging (i.e., >1 additional scan per year) was highest in year 3 (28%, 104/368).

Adherence with chest imaging was even lower (range 11–34% during years 1–5). Substantial underuse of chest imaging (i.e., >1 under-reported scan per year) was highest in year 1 and 2 (57% and 73%, respectively); substantial overuse of chest imaging (i.e., >1 additional scan per year) was relatively uncommon (range 1–12% in years 1–5).

#### Seminoma

As shown in Table 3, among patients with seminoma, adherence with abdominal and chest imaging was relatively stable and comparable throughout the 10-year followup period (range 23–47% abdomen and 28–47% chest). A substantial number of patients had underuse of abdominal imaging for seminoma (range 48–77%), with substantial underuse in 21–42%. There was very little overuse of abdominal imaging for seminoma. Chest imaging was more likely to be underand overused. Rates of underuse increased over time (from 14% in year 1 to 58% in year 10); overuse rates decreased over time (57% in year 1 to 10% in year 10).

#### Factors associated with under/overuse of imaging

Underuse of imaging was more common in later years (odds ratio [OR] per year 1.14, 95% confidence interval [CI] 1.06–1.23) and among those patients with NSGCT (OR 1.87, 95% CI 1.08–3.24) during years 1 and 2 (Table 4). These associations persisted in multivariate analysis (adjusted OR for years 1.15 [1.06–1.25] and for NSGCT histology 2.11 [1.01–4.38]). Patients with orchiectomy in later years were more likely to have underuse for years 3–5 as well (adjusted

Non-seminoma (n=56	9)				
			CT abdomen and pelvis		
Year	Concordant	Underuse	Substantial underuse	Overuse	Substantial overuse
Year 1 (n=432)	151 (35%)	239 (55%)	87 (20%)	42 (10%)	≤5
Year 2 (n=414)	108 (26%)	289 (70%)	148 (36%)	17 (4%)	≤5
Year 3 (n=368)	135 (37%)	NA	NA	233 (63%)	104 (28%)
Year 4 (n=323)	202 (62%)	NA	NA	121 (37%)	47 (14%)
Year 5 (n=286)	193 (67%)	NA	NA	93 (32%)	18 (6%)
			CT Chest or CXR		
Year 1 (n=432)	54 (12%)	301 (70%)	248 (57%)	77 (17.82%)	50 (11.57%)
Year 2 (n=414)	46 (11%)	354 (86%)	304 (73%)	14 (3.38%)	≤5
Year 3 (n=368)	91 (25%)	239 (65%)	137 (37%)	38 (10.33%)	11 (2.99%)
Year 4 (n=323)	109 (34%)	171 (53%)	89 (28%)	43 (13.31%)	7 (2.17%)
Year 5 (n=286)	93 (32%)	105 (37%)	NA	88 (30.77%)	11 (3.85%)
Seminoma (n=1107)					
			CT abdomen and pelvis		
Year 1 (n=906)	232 (26%)	657 (73%)	194 (21%)	17 (2%)	≤5
Year 2 (n=849)	348 (41%)	476 (56%)	212 (25%)	25 (3%)	≤5
Year 3 (n=731)	221 (30%)	498 (68%)	272 (37%)	12 (2%)	≤5
Year 4 (n=619)	291 (47%)	297 (48%)	152 (24)	31 (5%)	≤5
Year 5 (n=513)	215 (42%)	287 (56%)	154 (30%)	11 (2%)	≤5
Year 6 (n=418)	132 (32%)	281-285	135 (32%)	≤5	≤5
Year 7 (n=321)	73 (23%)	243-247	136 (42%)	≤5	≤5
Year 8 (n=248)	114 (46%)	120 (48%)	NA	14 (6%)	≤5
Year 9 (n=180)	84 (47%)	90 (50%)	NA	6 (3%)	≤5
Year 10 (n=124)	51 (41%)	68-73	NA	≤5	≤5
			CT chest or CXR		
Year 1 (n=906)	258 (28%)	128 (14%)	15 (2%)	520 (57%)	273 (30%)
Year 2 (n=849)	261 (31%)	420 (49%)	167 (20%)	168 (20%)	63 (7%)
Year 3 (n=731)	247 (34%)	216 (29%)	NA	268 (37%)	103 (14%)
Year 4 (n=619)	224 (36%)	218 (35%)	NA	177 (28%)	46 (7%)
Year 5 (n=513)	198 (39%)	189 (37%)	NA	126 (24%)	26 (5%)
Year 6 (n=418)	196 (47%)	163 (39%)	NA	59 (14%)	10 (2%)
Year 7 (n=321)	122 (38%)	161 (50%)	NA	38 (12%)	8 (2%)
Year 8 (n=248)	98 (39%)	128 (52%)	NA	22 (9%)	≤5
Year 9 (n=180)	84 (47%)	85 (47%)	NA	11 (6%)	≤5
Year 10 (n=124)	40 (32%)	72 (58%)	NA	12 (10%)	_• ≤5
	XR: chest X-ray; NA: not applicable				

### Table 3. Concordance with imaging among patients with testicular cancer treated with active surveillance in Ontario from 2000–2010

OR 1.09 [1.01–1.19]). Compared with seminoma, patients with NSGCT were less likely to have underuse during years 3–5 of followup (adjusted OR 0.53 [0.34–0.84]).

Overuse of imaging in years 1–2 was less common among patients with NSGCT (adjusted OR 0.24 [0.18–0.33]) (Table 5). During years 3–5, NSGCT was associated with higher odds of overuse (adjusted OR for NSGCT 4.01 [2.58–6.24]). For years 3–5, although low-risk disease was associated with overuse in the univariate analysis (OR 1.67 [1.23–2.27]), this did not persist when adjusted in the multivariable analysis.

There was substantial regional variation in overuse (range 50–100%) but not underuse (range 80–88%). In multivari-

able analysis, overuse was but underuse was not associated with geographical region both for years 1–2 and years 3–5.

#### Discussion

In this population-based study, we described use of imaging among patients with testicular cancer managed by AS. The study has highlighted substantial discordance with imaging guidelines. Our data show substantial rates of underuse and overuse that vary during the different phases of surveillance followup.

Cancer treatment must balance efficacy and toxicity. Treatment of testicular cancer is one of the success stories in

	Years 1–2			Years 3–5		
	Univariate analysis		Multivariate analysis	Univariate analysis		Multivariate analysis
	Rate	OR (95% CI)	OR (95% CI)	Rate	OR (95% CI)	OR (95% CI)
2000–2010^		1.14 (1.06–1.23)	1.15 (1.06–1.25)		1.07 (0.99–1.16)	1.09 (1.01–1.19)
Age						
<30 years	96	Ref	Ref	84	Ref	Ref
30–39 years	93	0.59 (0.33–1.07)	0.75 (0.39–1.46)	79	0.74 (0.48–1.13)	0.61 (0.37–0.99)
40+ years	92	0.56 (0.31–1)	0.63 (0.33-1.22)	82	0.89 (0.57–1.39)	0.69 (0.41–1.17)
Histology						
Non-sem	96	1.87 (1.08–3.24)	2.11 (1.01–4.38)	77	0.61 (0.43–0.88)	0.53 (0.34–0.84)
Seminoma	93	Ref	Ref	84	Ref	Ref
Risk*						
High	93	Ref	Ref	84	Ref	Ref
Low	94	1.29 (0.8–2.08)	1.14 (0.7–1.86)	81	0.81 (0.54–1.19)	0.9 (0.59–1.35)

Table 4. Factors associated with underuse of surveillance imaging among patients with early-stage testicular cancer in Ontario treated from 2000–2010

^Per year. \*High-risk disease is defined as: lymphovascular invasion for non-seminoma germ cell tumors, tumor>4 cm, and/or rete testis involvement for seminoma. Geographic region was included in the multivariate model but was not associated with imaging use. CI: confidence interval; OR: odds ratio.

oncology in which high rates of success have been achieved; recent focus in this disease has been to minimize the toxicity of therapy. High rates of cures are achievable in testicular cancer, but numerous de-escalation trials have proven that high cure rates could be maintained with less intense treatment. This is particularly true for stage I testicular cancer, in which upfront adjuvant radiation therapy (for seminoma) or retroperitoneal lymph node dissection/adjuvant chemotherapy (for NSGCT) has been largely replaced by AS. This practice was driven by the data, which showed excellent outcomes can be achieved with less intensive therapy while simultaneously reducing treatment-related toxicity.<sup>9</sup> AS is also shown to be the most cost-effective modality of treatment.<sup>10</sup> Our previous study using the same database has shown that AS is now the most common treatment strategy for patients with stage I testicular cancer in Ontario.<sup>3</sup>

However, AS requires structured followup to maintain its effectiveness.<sup>11</sup> Surveillance is able to achieve excellent survival in large part due to regular and frequent monitoring with imaging and serum tumor markers to detect early relapse. Indeed, up to 15–50% of patients with stage I nonseminoma, and 10–20% of patients with seminoma relapse after AS.<sup>12</sup> Therefore, cancer care guidelines, such as those by NCCN, ESMO, or Cancer Care Ontario (CCO), recommend chest and abdomen/pelvis imaging at various frequencies and intervals for up to five (non-seminoma) or 10 years (seminoma) post-orchiectomy.

Our study finds that in routine practice, patients with testicular cancer commonly receive imaging tests at a rate that is discordant with recommended guidelines. This finding raises several interesting questions and hypotheses. First, it shows the complexities of treating patients with cancer in

	Years 1–2			Years 3–5		
	Uni	variate analysis	Multivariate analysis		ivariate analysis	Multivariate analysis
	Rate	OR (95% CI)	OR (95% CI)	Rate	OR (95% CI)	OR (95% CI)
2000-2010^		1.01 (0.97–1.05)	0.97 (0.93–1.02)		0.96 (0.9–1.02)	0.94 (0.88–1.01)
Age						
<30 years	39	Ref	Ref	66	Ref	Ref
30–39 years	52	1.67 (1.27–2.19)	1.14 (0.83–1.56)	64	0.94 (0.66–1.33)	1.46 (0.96–2.21)
40+ years	56	1.97 (1.5–2.58)	1.1 (0.8–1.51)	58	0.72 (0.51–1.03)	1.08 (0.71–1.63)
Histology						
Non-sem	26	0.22 (0.17–0.29)	0.24 (0.18-0.33)	78	3.05 (2.19–4.25)	4.01 (2.58–6.24)
Seminoma	61	Ref	Ref	54	Ref	Ref
Risk*						
High	54	Ref	Ref	55	Ref	Ref
Low	49	0.8 (0.64–1.01)	1.02 (0.79–1.31)	67	1.67 (1.23–2.27)	1.38 (0.99–1.92)

 Table 5. Factors associated with overuse of surveillance imaging among patients with early-stage testicular cancer in

 Ontario treated from 2000–2010

^Per year. \*High-risk disease is defined as: lymphovascular invasion for non-seminoma germ cell tumors, tumor >4 cm, and/or rete testis involvement for seminoma. Geographic region was included in the multivariate model and was significantly associated with imaging overuse both in years 1–2 and years 3–5 (data not shown). CI: confidence interval; OR: odds ratio.

the real-world setting. Delivery of guideline-based care for testicular cancer is very important because most patients (even with advanced disease) can be cured. However, our study identifies important gaps with care delivery in routine practice. We found that rates of discordance (and whether it was under or overuse) were largely related to the number of years from orchiectomy. This likely reflects changes in clinical practice (i.e., clinicians might be more or less likely to order tests), as well as the fact that guidelines have different levels of imaging intensity during the years of followup. We also observed significant variation across regions, especially with regards to overuse, which is not surprising, as practice patterns in this context will vary from center to center.

Second, the guidelines for frequency of imaging during AS for testicular cancers are based on consensus, informed by data regarding the timing of relapse following orchidectomy. That may also explain why the physicians are not rigorous in following the guideline recommendations with regards to surveillance protocol for imaging; it may also reflect the fact that the disease remains highly curable even when advanced. There are also patient-related factors that may explain the lack of adherence to surveillance guidelines. The patient population for testicular cancers is unique in that the cohort comprises mostly of young men who are working, mobile, and may not routinely adhere to the surveillance protocol.

Third, our study suggests that overuse of imaging is very common, particularly for chest imaging in the early years of seminoma and body imaging in the later years for NSGCT. Overuse of imaging has its downstream hazards, including excessive exposure to radiation and detection of indeterminate lesions leading to downstream invasive diagnostic and therapeutic procedures. Over-imaging, and all these downstream cascades of medical interventions, also incur substantial costs to the payer.

An important question that arises from our study is whether underuse of imaging during surveillance leads to inferior outcomes. While existing datasets and methodological limitations do not allow for a definitive answer to this question, it is notable that despite substantial imaging underuse, the outcomes of patients treated with surveillance in Ontario is excellent. A seminal clinical trial report published in 2007 suggested that two CT scans, as opposed to five, did not compromise outcomes in patients with low-risk stage I NSGCT.<sup>13</sup> New data from the TRISST trial also shows non-inferiority of three scans during surveillance (at months six, 18, and 36) compared with seven scans (at months six, 12, 18, 24, 36, 48, and 60) among patients with stage I seminoma and suggests imaging maybe unnecessary beyond three years.<sup>14</sup> Despite the detection of underuse and overuse of imaging in our study, our previous study using the same cohort of patients as this study revealed a five-year survival rate of 97% and cancer-specific survival of 98%, which is consistent with global data.<sup>3</sup> However, our data do not support purposeful delivery of care that is not consistent with guidelines. Future studies should focus on further reducing unnecessary imaging to this population.

Our study should be interpreted in light of methodological limitations. Existing datasets do not include stage of disease or serum tumor markers. Accordingly, we defined patients on AS as those patients treated with orchiectomy and no further radiation therapy/chemotherapy/ retroperitoneal lymph node dissection within the subsequent 90 days. Lack of information regarding tumor markers and indication for imaging means we do not know if radiographical investigations were performed in response to new symptoms (or rising tumor markers), followup of prior equivocal findings, or were planned as per routine surveillance; this means that some apparent overuse may, in fact, be appropriate. One way to address this would have been to censor patients a certain number of days or at the penultimate scans before they re-started any treatment, but there is no agreement on the ideal number of days and these approaches are also at risk of falsely under-reporting surveillance scans. We have also not reported imaging use beyond the usual surveillance periods (five years for NSGCT and 10 years for seminoma); accordingly we may underestimate overuse of imaging, as some patients may continue to have routine tests beyond the recommended time frames. To measure the extent to which practice was concordant with contemporaneous guidelines, we compared imaging frequency to guidelines from an earlier era, which were published by Ontario's largest cancer center. While many oncologists in Ontario used these guidelines at that time, this may limit the extent to which these findings apply to the current era. Finally, our study design does not account for patients lost to followup entirely and for whom we have no further information about imaging after year 1.

#### Conclusions

This study illustrates that use of surveillance imaging among patients with early-stage testicular cancer is frequently discordant with guideline recommendations. We have observed substantial under- and overuse. Future clinical trials should evaluate whether imaging protocols can be safely de-escalated and how to reduce unnecessary overuse of imaging.

**Competing interests:** Dr. Gyawali has received consulting fees from Vivio Health. Dr. Robinson has received honoraria from Merck; consulting fees from Amgen, AstraZeneca, and Merck; and research funding from AstraZeneca, BMS, Merck, and Roche. Dr. Bedard has received consulting fees from Amgen, BMS, Lilly, Merck, Pfizer, and Seattle Genetics; and has received research funding for his institution from Amgen, AstraZeneca, Bicara, BMS, Genetech/Roche, GSK, Immunomedics, Lilly, Merck, Mersana, Nektar, Novartis, PTC Therapeutics, Sanofi, Seattle Genetics, and Servier. The remaining authors do not report any competing personal or financial interests related to this work.

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#### References

- Gilligan T, Lin DW, Aggarwal R, et al. Testicular cancer, version 2.2020, NCCN clinical practice guidelines in oncology. J Natl Compr Canc Netw 2019;17:1529-54. https://doi.org/10.6004/jnccn.2019.0058
- Oldenburg J, Fosså SD, Nuver J, et al. Testicular seminoma and non-seminoma: ESMO clinical practice guidelines for diagnosis, treatment and followup. *Ann Oncol* 2013;24:vi125-32. https://doi.org/10.1093/ annonc/mdt304
- Leveridge MJ, Siemens DR, Brennan K, et al. Temporal trends in management and outcomes of testicular cancer: A population-based study. *Cancer* 2018;124:2724-32. https://doi.org/10.1002/cncr.31390
- Ernst DS, Brasher P, Venner PM, et al. Compliance and outcome of patients with stage 1 non-seminomatous germ cell tumors (NSGCT) managed with surveillance programs in seven Canadian centers. Can J Urol 2005;12:2575-80. https://pubmed.ncbi.nlm.nih.gov/15877938/
- Booth CM, Mackillop WJ. Translating new medical therapies into societal benefit: The role of populationbased outcome studies. JAMA 2008;300:2177-9. https://doi.org/10.1001/jama.300.18.2177
- Booth CM, Karim S, Mackillop WJ. Real-world data: Towards achieving the achievable in cancer care. Nat Rev Clin Oncol 2019;16:312-25. https://doi.org/10.1038/s41571-019-0167-7
- von Elm E, Altman DG, Egger M, et al. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: Guidelines for reporting observational studies. Int J Surg 2014;12:1495-19. https://doi.org/10.1016/j.ijsu.2014.07.013

- Clarke EA, Marrett LD, Kreiger N. Cancer registration in Ontario: A computer approach. *IARC Sci Publ* 1991:246-57. https://pubmed.ncbi.nlm.nih.gov/1894327/
- Pierorazio PM, Cheaib JG, Patel HD, et al. Comparative effectiveness of surveillance, primary chemotherapy, radiotherapy, and retroperitoneal lymph node dissection for the management of early-stage testicular germ cell tumors: A systematic review. J Urol 2021;205:370-82. https://doi.org/10.1097/ ju.000000000001364
- Huang MM, Su ZT, Cheaib JG, et al. Cost-effectiveness analysis of non-risk-adapted active surveillance for post-orchiectomy management of clinical stage I seminoma. *Eur Urol Focus* 2020:S2405-4569(20)30170-X. https://doi.org/10.1016/j.euf.2020.06.012
- Kollmannsberger C, Tyldesley S, Moore C, et al. Evolution in management of testicular seminoma: population-based outcomes with selective utilization of active therapies. *Ann Oncol* 2011;22:808-14. https://doi.org/10.1093/annonc/mdq466
- Nappi L, Nichols CR, Kollmannsberger CK. New treatments for stage I testicular cancer. *Clin Adv Hematol Oncol* 2017;15:626-31. https://pubmed.ncbi.nlm.nih.gov/28949950/
- Rustin GJ, Mead GM, Stenning SP, et al. Randomized trial of two or five computed tomography scans in the surveillance of patients with stage I non-seminomatous germ cell tumors of the testis: Medical Research Council Trial TEO8, ISRCTN56475197 — the National Cancer Research Institute Testis Cancer Clinical Studies Group. J Clin Oncol 2007;25:1310-5. https://doi.org/10.1200/JC0.2006.08.4889
- Joffe JK, Cafferty FH, Murphy L, et al. Imaging modality and frequency in surveillance of stage I seminoma testicular cancer: Results from a randomized, phase 3, factorial trial (TRISST). J Clin Oncol 2021;39:374. https://doi.org/10.1200/JC0.2021.39.6\_suppl.374

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