Accuracy of germ cell tumor histology and stage within a Canadian cancer registry

Patrick Holland[1,2], Efthimios Karmas[3], Jennifer Merrimen[2,4], Lori A. Wood[2,5,6]
[1]Department of Medicine, Dalhousie University, Halifax, NS, Canada; [2]QEII Health Sciences Centre, Nova Scotia Health, Halifax, NS, Canada; [3]Dalhousie University, Halifax, NS, Canada; [4]Department of Pathology, Dalhousie University, Halifax, NS, Canada; [5]Department of Urology, Dalhousie University, Halifax, NS, Canada; [6]Division of Medical Oncology, Department of Medicine, Dalhousie University, Halifax, NS, Canada

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Corresponding author: Dr. Patrick Holland, Department of Medicine, Dalhousie University, Halifax, NS, Canada; PHolland@dal.ca

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ABSTRACT

Introduction: Cancer registries are the mainstay for Canadian population-based cancer statistics. Data are collected in provincial and territorial registries, including the Nova Scotia Cancer Registry (NSCR). The goal of this study was to determine the accuracy of NSCR data for germ cell tumors (GCT).

Methods: This analysis included all NSCR patients diagnosed with GCT from 2006–2015. The date and method of diagnosis, primary site, histology, and stage were recorded from the NSCR and compared to each patient's chart. Any discrepancies between the two sources were reviewed and reasons behind the discrepancies recorded.

Results: A total of 229 patients made up the study cohort. Using NSCR data, 57.6% had seminoma, 34.5% non-seminoma (NSGCT), and 7.9% other. Discrepancies in pathology were noted in 16 patients (7.0%). Using NSCR staging data (available in 185 cases), 71.9% had stage I, 12.4% stage II, 11.9% stage III, and 3.8% other. Discrepancies in stage were noted in 32 patients (17.3%) with NSCR data downstaging 8 patients (4.3%) and upstaging 21 patients (11.4%). The site of the primary GCT was discrepant in 12 patients (5.2%). The date of diagnosis was accurate within one week for all patients except one.

Conclusions: Higher-level NSCR data, such as date of diagnosis and overall pathological diagnosis, appear relatively accurate; however, there are inaccuracies in histological subtype and stage within the NSCR. Regular discussion between registry personnel, clinicians, pathologists, and researchers is required for accurate data reporting.

KEY MESSAGES

- Nova Scotia Cancer Registry data for germ cell tumors on date of diagnosis and overall pathological diagnosis are relatively accurate.
- Within the NSCR, there are significant inaccuracies in reporting of histological subtype and stage.
- Regular discussion between registry personnel, clinicians, pathologists, and researchers is required for accurate data reporting.

and stage. This study raises awareness of these gaps and highlights key areas for improvement in educating registry personnel who interpret and enter data about the uniqueness of GCT pathology, staging, and interpretation of tumor markers.

INTRODUCTION

Canadian cancer statistics are published annually by the Canadian Cancer Statistics Advisory Committee in collaboration with the Canadian Cancer Society, Statistics Canada and the Public Health Agency of Canada with data provided by the provincial and territorial cancer registries (PTCR).[1] Each PTCR, including the Nova Scotia Cancer Registry (NSCR), captures and submits their own data on every cancer diagnosis identified through pathology reports and cancer centre registrations. These data are then used nationally and provincially in many capacities including developing cancer control strategies and research. Thus, it is vital that registry data contain accurate information, and if not, to understand why that may be the case.

Testicular cancers are a rare cancer with only 1200 cases projected to be diagnosed in Canada in 2021, but are the most common cause of cancer in males between the ages of 16 and 35 years.[1] Histologically, 95% are germ cell tumors (GCT) that are largely classified as seminomas, or non-seminomatous germ cell tumors (NSGCT). NSCGT can include tumors comprised of a single non-seminomatous subtype, however they can also include a mixture of seminoma and non-seminomatous histology, or multiple subtypes of non-seminoma.[2] GCT can arise in any midline structure, including the pineal gland (often referred to as germinoma), mediastinum, and retroperitoneum. Prognosis and management of GCTs differs significantly depending on the histology and stage, therefore it is important that Canadian registry data are accurate and reliable to use. Given the low incidence of GCT, even minor inaccuracies may have a big impact in terms of research and planning.

The objectives of this study were to determine the accuracy of NSCR data regarding the diagnosis, primary site, histological subtype, and stage of GCT by comparing NSCR data with individual pathology reports and staging investigations from the chart. When discrepancies existed, the secondary goal was to determine the reason why, in the hopes of improving data quality, interpretation, and collection in the future.

METHODS

Approval for this study was obtained from the Nova Scotia Health Research Ethics Board. Data from unique male GCT cases in the NSCR over a 10 year period between January 1, 2006 and December 31, 2015 were recorded. GCT cases were identified using the ICD-O histology codes (9061/3, 9062/3, 9064/3, 9065/3, 9070/3, 9071/3, 9085/3, 9080/3) and the ICD-O site codes (62.0, 62.1, 62.9, 38.1, 80.9, 75.3, 48).[3] Patients aged 16 years or older were included as the majority of 16-18 year olds in Nova Scotia were managed at adult cancer centres.

NSCR variables including date of diagnosis, method of diagnosis, histology, stage at diagnosis, and site of origin were recorded. These same variables were extracted from the

patients' medical records. If synchronous testicular cancers were diagnosed, the pathology that required the most aggressive management was recorded.

Discrepancies between the NSCR and the medical record histology reports were recorded and reviewed by 2 authors independently (PH & LW). In the case of disagreement between the authors, the NSCR and chart data were re-reviewed along with the relevant literature. All disagreements were resolved following these measures. Discrepancies between the NSCR and medical records were then determined to be clinically significant (eg. seminoma to NSGCT, or stage IIa to IIb) or not clinically significant (eg. pure embryonal to mixed NSGCT, or stage Ia to Ib). For all clinically significant discrepancies, the reason was recorded. If all data required to accurately collect the information were available in the chart but not interpreted correctly, the reason for the discrepancy was recorded as misinterpretation by coder (eg. coding Stage IS despite normalization of tumor markers post orchiectomy). True coding error was defined as incorrect data entry despite clear evidence in the chart (eg. stage IV disease). If there was no appropriate coding option within the NSCR this was noted.

Statistics

Variables were entered into a secure REDCap database. Clinical characteristics were summarised using means and standard deviations for continuous variables, and frequency and counts for categorical variables.

RESULTS

During the study period, 239 unique patients with a diagnosis of GCT were identified in the NSCR. 10 patients were excluded as they had key investigations or management in other provinces, therefore complete data for verification could not be obtained. The incidence was consistent with a median of 22 cases per year (range 18 - 31). The median age was 35 years (range 16 – 94). All cases occurred in male patients. Baseline NSCR characteristics are displayed in Table 1.

Date of diagnosis

The NSCR date of diagnosis was discrepant in 3 patients. The discrepancy was less than 7 days in 2 patients, both of which were diagnosed by tumor markers and imaging, and not histology. There was a discrepancy of 18 months in 1 patient which appeared to be a true coding error.

Site of primary

From the NSCR, the primary site was testicular in 221 (96.5%), retroperitoneal in 1 (0.4%), mediastinal in 2 (0.9%), pineal gland in 2 (0.9%), and unknown in 3 (1.3%) as shown in Table 2. The site of primary was discrepant in 12 patients (5.2%). In 9 of these patients, the NSCR recorded testis or unknown as the primary site, whereas these patients had a post chemotherapy orchiectomy, which is not an option in the NSCR. In 2 patients, the NSCR recorded testis as the primary site whereas the patients had burnt out primaries, which is not a coding option in the NSCR. In 1 patient, the NSCR recorded the primary site to be unknown whereas the patient had a mediastinal primary which represents a misinterpretation by the coder.

Histology

From the NSCR, patients were diagnosed with GCT based on orchiectomy in 205 (89.5%), retroperitoneal lymph node (RPLN) biopsy in 12 (5.2%), biopsies of other sites in 10 (4.4%), and tumor markers and radiological imaging in 2 (0.9%).

From the NSCR, the diagnosis was seminoma in 132 patients (57.6%), NSGCT in 79 patients (34.5%), germinoma in 10 patients (4.4%), spermatocytic seminoma in 5 patients (2.2%) and other in 3 patients (1.3%) as shown in Table 3.

Of the 132 NSCR seminoma patients, 3 were misclassified (2.3%) and should have been NSGCT in 2 and spermatocytic seminoma in 1. Of the 79 NSCR NSGCT patients, 1 was misclassified (1.3%) and should have been seminoma. Of the 10 NSCR germinomas, 8 were misclassified (80%) and should have been seminoma in 2 and NSGCT in 6. Of the 5 NSCR spermatocytic seminomas, 1 was misclassified (20%) and should have been a sarcomatoid neoplasm. Of the 3 NSCR other diagnoses (anaplastic seminoma and teratocarcinoma), all 3 (100%) were misclassified and should have been NSGCT.

Clinically significant histological discrepancies were noted in 16 patients as shown in Table 4. Half of these discrepancies were misclassified as germinoma, and in 6 of these patients, the diagnosis was made by biopsy (2 retroperitoneal masses and 4 other sites). In 2of the sixteen patients, the discrepancy was due to the fact that the pathology review at the tertiary centre was not recorded, but instead a provisional diagnosis was used, despite the pathology reports clearly indicating a pathology review was being requested. Other discrepancies included misinterpretation by coder in 3 cases (synchronous tumors where the largest tumor histology was recorded, a mixed tumor with predominant seminoma component recorded as seminoma, and misinterpretation of syncytiotrophoblasts in a patient with seminoma), and true coding error in 2 cases (recording the histology as teratocarcinoma despite that term not being mentioned on the pathology report).

Within the NSCR NSGCT category, 22 were reported as having a pure histology and 57 mixed. Many of these patients were misclassified as having a pure NSGCT when it should have been a mixed NSGCT. However, because this was unlikely to be clinically relevant, statistics and reasons for discrepancies are not reported. If stage I risk adapted treatment strategies were to become the standard in Canada, this issue may become clinically relevant.

Stage

The NSCR began recording stage data in 2008, therefore stage comparison was possible in 185 patients. As shown in Table 5, NSCR data showed stage I in 114 (61.6%), Stage IS in 19 (10.3%), stage II in 23 (12.4%), stage III in 22 (11.9%), stage IV in 1 (0.5%), not applicable and unknown in 6 (3.2%). On review of the chart data, stage I was present in 127 (68.6%), stage IS in 0 (0%), stage II in 26 (14.1%), stage III in 28 (15.1%), and not applicable (mediastinal or pineal primary) in 4 (2.2%). There were a total of 32 clinically relevant discordant stages as shown in Table 6. The reason for the discordance was not obvious in 28 patients (87.5%) as all of the data appeared to be present, other reasons in 3 (9.3%), and true coding error in 1 (3.1%). The stage obtained from chart review resulted in the NSCR upstaging 21 patients and downstaging 8 patients where the misclassification could have had

implications on treatment decisions; there was no potential effect on treatment decisions in 3 cases.

The most common reason for clinically relevant discordance appeared to be inappropriate coding of stage I tumors as stage IS in 18 cases (56%). On chart review, it appears that only pre-orchiectomy tumor markers were considered in these cases. In most of the other clinically relevant discrepancies, investigations required to correctly stage the patient were available and there was no apparent reason for misclassification.

DISCUSSION

GCT histology is more complex than other cancers for many reasons including mixed histologies, synchronous tumours, the need to interpret tumor markers in the absence of pathology or with a needle biopsy only, and dedifferentiation of GCT. Staging of GCT utilising the AJCC TNM criteria is also complex.[4] For example, it requires specific information on retroperitoneal lymph node size and tumor marker elevation not only at diagnosis in advanced patients, but post-orchiectomy in localized patients. This complexity makes reporting, coding and recording in cancer registries more difficult.

With regards to histology, discordance occurred in 7% of patients. When categorizing patients between seminoma and NSGCT, the registry data were relatively accurate, but not completely. Inaccuracies occurred in more granular details and rarer entities. For example, the NSCR data coded 10 patients as germinoma, a term which should only be applied to pineal gland GCT of which there were only 2 patients on chart review; the other 8 were NSGCT. Within the NSGCT category, the NSCR data were not accurate in classifying pure and mixed histologies. The NSCR also does not allow for more detailed information to be recorded such as spermatocytic seminoma with sarcomatous elements, or mixed GCT with carcinoid elements which may result in different treatment strategies and outcomes.

With regard to stage, discordance occurred in 17.3% of patients with the NSCR upstaging 11.4% and downstaging 4.3% of cases. The most common discrepancy was NSCR recording stage IS (which would require systemic treatment) when in fact the tumor was stage I (where surveillance is the most appropriate management).

From this review, we were able to identify key areas to target education for registry coders to immediately improve the accuracy of data. For example, in terms of histology, clarifying the definition of germinoma would eliminate half of the identified errors. As well, education on how to interpret elevated tumour markers in the setting of a needle biopsy or no biopsy (eg. βHCG >5000 IU/L or any abnormal AFP should be coded as NSGCT)[5] would be helpful, along with the knowledge that the term teratocarcinoma is outdated and that the predominant histology is not always the one to record. With regards to the stage, over half of the discrepancies could be resolved with specific coder education around the definition of stage IS disease and the need to follow the tumour markers post-orchiectomy. Other areas for education around stage include: understanding that stage IV does not exist for GCT, recognizing the mediastinum as a primary site, and knowing that pelvic lymph nodes do not represent regional lymph nodes.

Given that histopathological terminology and staging do evolve over time, it is important to update categories within the registry and educate registry coders with respect to

those changes. For example, although the term spermatocytic seminoma was used within the NSCR during the study period, the correct terminology is now spermatocytic tumor.[6] While only one case of retroperitoneal primary GCT was reported in this cohort, the evidence suggests that this entity may not actually exist and that these tumors represent metastatic spread from a testis primary where the only remaining evidence may be scar.[7]

The discrepancies between the NSCR and chart data may not appear large in absolute numbers, but in a cancer where the Canadian incidence is only 1,200 cases per year, even small misclassifications may be significant. For example, if one wanted to look at stage migration during the COVID-19 pandemic (with the hypothesis that patients presented with more advanced disease), one would have to be aware of these discrepancies.

Thus, we propose targeted education to registry coders which would result in an immediate elimination in over half of the histology and stage inaccuracies. Ongoing dialogue between clinicians, pathologists, researchers and registry personnel is imperative and must occur on a regular basis.

CONCLUSIONS

Knowing the correct diagnosis, histological subtype, and stage for a rare cancer like GCT is imperative for managing GCT patients, as well as improving care through research and innovation. This research highlights the need for active and ongoing discussions between the registry community and the clinicians, pathologists, and researchers using and relying on this data.

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Figures and Tables

Table 1. Baseline NSCR characteristics	
	n (%)
Study cohort	229
Median age at diagnosis (years)	35 (16–94)
Median incidence (cases/year)	22 (18–31)
Method of diagnosis	
Orchiectomy	205 (89.5)
Biopsy/RPLND	22 (9.6)
Radiological & tumor markers	2 (0.9)

NSCR: Nova Scotia Cancer Registry; RPLND: retroperitoneal lymph node dissection.

Table 2. Site of primary tumor (n=229)		
	NSCR (%)	**Chart (%)**
Testicular	221 (96.5)	211 (92.4)
Retroperitoneal	1 (0.4)	1 (0.4)
Mediastinal	2 (0.9)	3 (1.3)
Pineal gland	2 (0.9)	2 (0.9)
Unknown/other	3 (1.3)	12 (5.2)*

*11 had orchiectomy with no cancer found, either post chemotherapy or presumed burnt-out primary.

Table 3. Comparison of NSCR to chart histology (n=229)			
	NSCR path (%)		**Chart path (%)**
Seminoma	132 (57.6)	→ 3 incorrectly coded as seminoma (2 NSGCT, 1 spermatocytic seminoma) ← 3 incorrectly coded and should be seminoma (2 germinoma, 1 NSGCT)	132 (57.6)
NSGCT	79 (34.5)	→ 1 incorrectly coded as NSGCT (1 seminoma) ← 11 incorrectly coded and should be NSGCT (6 germinoma, 2 seminoma, 1 anaplastic seminoma and 2 teratocarcinoma/other)	89 (38.9)
Germinoma	10 (4.4)	→ 8 incorrectly coded as germinoma (2 seminoma and 6 NSGCT)	2 (0.9)
Spermatocytic seminoma	5 (2.2)	→ 1 incorrectly coded as spermatocytic seminoma (sarcomatoid neoplasm/other) ← 1 incorrectly coded as seminoma	5* (2.2)
Other	3 (1.3)	→ 2 incorrectly coded as teratocarcinoma (2 NSGCT) → 1 incorrectly coded as anaplastic seminoma (NSGCT) ← 1 incorrectly coded as spermatocytic seminoma (1 sarcomatoid neoplasm)	1 (0.4)

*Including with dedifferentiation which was not coded. NSCR: Nova Scotia Cancer Registry; NSGCT: non-seminoma germ cell tumor.

Table 4. Clinically relevant differences in histology				
Reason for discordance				
Total discordant	**Coded as germinona**	**Pathology review not incorporated**	**No appropriate coding option**	**Misinterpretation/ True coding error**
16	8	2	1*	5**

*Sarcomatoid neoplasm. **3 misinterpretation by coder, and 2 true coding errors.

Table 5. Comparison of stage at diagnosis (n=185)		
Stage	**NSCR (%)**	**Chart (%)**
I IS	114 (61.6) 19 (10.3)	127 (68.6) 0 (0)
II	23 (12.4)	26 (14.1)
III	22 (11.9)	28 (15.1)
Other*	7 (3.8)	4 (2.2)

*Includes stage IV, NA, Unknown. NSCR: Nova Scotia Cancer Registry.

Table 6. Clinically relevant differences in stage			
Reason for discordance			
Total # discordant	**Misinterpretation of stage IS**	**Other misinterpretation**	**True coding error**
32	18	13	1*

*Nova Scotia Cancer Registry listed as stage IV.