Tumor Registry Versus Physician Medical Record Review: A Direct Comparison of Patients With Pancreatic Neuroendocrine Tumors

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Abstract

Purpose: Tumor registry (TR) data are becoming more prominently cited in research through increased use of the National Cancer Database. We aimed to establish the accuracy of TR data by comparing them with physician medical record review (MD review) using pancreatic neuroendocrine tumors (NETs) as an example.

Methods: For MD review, the health information system of an academic medical center was queried for patients with pancreatic International Classification of Diseases, ninth revision (ICD-9), codes from January 2000 to August 2008. A single physician investigator analyzed those medical records and identified patients with pancreatic NETs. For TR data, patients with pancreatic NETs were identified by two separate strategies. For the period of January 2000 to December 2006, patients were identified through manual review of pathology reports, admission and discharge sheets, and clinic visit logs. For January 2007 to Au-

gust 2008, patients were identified using an automated case-finding program.

Results: In MD review, 1,192 patients with pancreatic ICD-9 codes were identified, 34 of whom were found to have pancreatic NETs. The TR indicated 15 patients with pancreatic NETs, four of whom were not identified during MD review. Of the total 38 patients identified by either strategy, pancreatic NET identification rate of the TR was 39.5% compared with 89.5% in MD review.

Conclusion: Academic TR analysis indicates a substantial proportion of patients with pancreatic NETs are not identified when compared with MD review. Most instances of patients going unidentified are the result of registry time lag and case-finding methodologies; specifically, physicians may define tumors with malignant potential differently. This may be applicable to other individual tumor registries as well as aggregate registry-based national studies.

Introduction

Historically, cancer researchers have underutilized tumor registry (TR) data, instead using medical record review and/or personal or institutional databases to identify patients with particular malignancies. However, TR data are becoming increasingly prominent on a national level through broader use of the National Cancer Database (NCDB).¹⁻⁴

Pancreatic neuroendocrine tumors (NETs) are a rare subtype of pancreatic neoplasms with an extended natural history,⁵ thought to arise either from well-differentiated mature endocrine cells or pancreatic multipotent stem cells. They are associated with genetic disorders such as multiple endocrine neoplasia I, von Hippel-Lindau syndrome, neurofibromatosis type I, and tuberous sclerosis. They are divided clinically into functioning and nonfunctioning tumors. Functioning tumors cause clinical endocrinopathy resulting from the inappropriate secretion of hormones. A majority of pancreatic NETs, although slow progressing, are considered to be malignant and metastasize predominantly to the liver.

The 2004 WHO classification has been used to differentiate pancreatic NETs with benign features from those that are malignant or have malignant potential.⁶ However, the differentiation of pancreatic NETs into benign and malignant categories is controversial, because some pancreatic NETs classically thought to be benign still have the ability to invade adjacent structures and metastasize if left untreated.⁷ Moreover, current histologic coding systems required to be used by all cancer

registries (ie, International Classification of Diseases for Oncology, third revision [ICD-O-3],⁸ and International Classification of Diseases, ninth revision [ICD-9],⁹ medical record coding system) have not kept pace with scientific progress in the understanding of the natural history of pancreatic NETs or with the updated 2004 WHO classification system.

Retrospective studies have been used to analyze TR data and gain insight into clinicopathologic and epidemiologic information for a variety of tumors.¹⁰⁻¹³ We hypothesized that pancreatic NETs could serve as an example to compare the accuracy of TR identification of these rare tumors with physician medical record review (MD review).

Methods

MD Review

The main criteria used by the physician reviewer for identifying patients with pancreatic NETs in the study were pathologic evidence of pancreatic neuroendocrine disease in electronic or paper records and exclusion of other possible diagnoses. The first step in this process was a request to the hospital information systems (HIS) department at our university hospital for a search identifying all patients within the electronic medical record system that had been coded with one or more of the following pancreatic ICD-9 codes: 157.0 to 157.9 and 211.6 to 211.7. Patient records from January 2000 (date current medical record system was put in place) to August 2008 (when physician

reviewer started study) were obtained. Electronic records of all identified patients were reviewed and separated into true pancreatic diagnoses (any type of pancreatic disease) and diagnoses that had been incorrectly coded with a pancreatic code. Full electronic record review followed for patients with all true pancreatic diagnoses to identify those with NETs. The paper records of these patients with NETs were further reviewed to exclude other possible diagnoses. A request for exemption was completed and approved by the institutional review board before initiation of the study.

TR Data

TR data were collected from the same institution for the same time period. The TR is part of the University of Massachusetts Accredited Cancer Program, accredited by the American College of Surgeons Commission on Cancer. As part of this program, TR data are directly submitted to the NCDB yearly, meeting all NCDB timeliness and data quality criteria. Additionally, the registry meets all federal and state requirements mandating that incidences of cancer diagnosed and/or treated in our medical center be reported to the Massachusetts State Cancer Registry, which in turn reports to the Centers for Disease Control. The Massachusetts State Cancer Registry was awarded the North American Association of Central Cancer Registries (NAACCR) Gold Standard for quality, completeness, and timeliness.

Patients with pancreatic NETs are classified in the TR on the basis of ICD-O-3 codes (8246/3, neuroendocrine carcinoma, or 8240/3, malignant carcinoid tumor). Cases that are defined as malignant by this coding system are recorded within the TR per the reportability standards of the NAACCR.

For collection of TR data in this study, patients diagnosed with pancreatic NETs were identified using the TR electronic database with assistance of the staff registrars. Of note, during the course of this study, there was a change in the case-finding methodology. From January 2000 to December 2006, TR staff used manual record review to identify patients with malignant tumors to include in the registry. Patients were identified by diagnosis codes from review of pathology reports, admission and discharge sheets, and clinic records. Starting in January 2007 and continuing through August 2008, an automated case-finding program—Cancer Alert System (CAS; C/NET Solutions, Berkeley, CA)—was used to identify patients with cancer. The CAS case-finding engine scans electronic medical records for 3,000 specific words related to malignancy. The registrars receive the automated reports, scan through the data provided by CAS, and remove negative cases, if necessary. In previous studies, automated case-finding programs have been found to be less time consuming and more accurate than manual review in identifying patients with cancer and capturing relevant information in the TR.¹⁴

Blinded Review

All MD review- and TR-identified patients with pancreatic NETs were further reviewed by a second physician investigator

blinded to identification strategy to assure consistency of pancreatic NET definition.

Tumor Characteristics

Tumors were classified as functioning if records indicated symptoms resulting from excess release of hormones (eg, insulin, glucagon, vasoactive intestinal peptide, gastrin, somatostatin) or positive stains in the pathology report. Tumors were classified as nonfunctioning if records indicated that tumors either did not produce symptoms or did not stain or if there was lack of any report of tumor functionality.

Data Analysis

Initial analysis of all patients with HIS-identified pancreatic ICD-9 codes was conducted using Statistical Package for the Social Sciences (SPSS 17.0.0, Chicago, IL). All patients were categorized based on diagnosis as identified by physician computer-based medical record review. Patients with pancreatic NETs identified by MD review were then entered into a Microsoft Office 2003 Excel (Microsoft, Redmond, WA) spreadsheet and further categorized by tumor location, WHO classification, functioning status of the tumor, sex, age, and date of diagnosis. Patients with nonpancreatic NETs were excluded after closer examination via paper medical record review. Patients with pancreatic NETs identified by MD review were then compared with those identified by the TR. To evaluate the accuracy of TR compared with MD review, frequencies and percentages were examined on the basis of various patient (age, sex) and tumor characteristics (location, WHO classification, functionality).

Results

MD Review

HIS scanning for pancreatic ICD-9 codes identified 1,192 patients. Electronic records of all identified patients were reviewed, and 662 patients were determined to have true pancreatic diagnoses; the other 530 cases had been incorrectly coded with or incorrectly identified as having a pancreatic code and were then excluded. Full electronic record review was conducted for all patients with true pancreatic diagnoses. From that review, 50 (4.2%) patients with pancreatic NETs were identified. The paper records of these patients with NETs were further reviewed to exclude other possible diagnoses; an additional 16 patients were excluded because of presence of other NET diagnoses (four patients with duodenal, breast, or lung disease), diagnosis before 2000 (seven patients), or inconclusive diagnoses (five patients; Fig 1).

TR Data

Across the time period of the study, including both case-finding methodologies, the institutional TR identified a total of 15 patients with pancreatic NETs. Eleven were identified during the first time period (January 2000 to December 2006) and four during the second time period (January 2007 to August 2008).

Figure 1. Physician medical record review process for identification of patients with NETs. HIS, health information system; NET, neuroendocrine tumor; PNET, pancreatic neuroendocrine tumor.

Comparison of MD Review and TR Data

In comparison with the 34 patients identified by MD review, there were 15 patients identified by the TR, four of whom were not identified in MD review; 11 patients overlapped. Over the course of the study, the TR identified 15 (39.5%) of 38 patients, whereas MD review identified 34 (89.5%) of 38. Patient and tumor characteristics of those identified are described in Table 1.

Of the four patients missed by MD review, three were not listed in the initial HIS list of 1,192 patients, and one was included in the initial list but excluded by the MD reviewer because of a missing report from an outside hospital. Of the three patients missed in the initial HIS review, one had been coded adequately with the 157.9 pancreatic code, and the remaining two had not been coded with any of the pancreatic ICD-9 codes.

Follow-Up With the Institutional TR and Cancer Committee

Follow-up with the institutional TR in December 2009 (1 year after initial study) revealed that eight additional patients had been added to the TR by continuation of the electronic case-finding method. These patients were accounted for by the lag time associated with the processing of medical records and entering of data into the TR database; the TR estimated this lag time to be approximately 6.3 months. These eight patients had previously been identified by MD review. There were 14 other patients who had been identified by MD review but not identified by the TR as malignant cases. Three of these patients were identified by the TR as truly missed patients with malignant pancreatic NETs and were added. The remaining 11 patients were not included in the registry because their NETs were de-

finied as benign per WHO ICD-O-3 coding and thus not reportable per NAACCR standards (Table 2).

After discussion with the tumor registry regarding the incongruent patients counts, it became clear that the incidence of the majority of unmatched patients was the result of differences in definitions of pancreatic NETs. Per the definitions used by the physician reviewer to identify all patients with pancreatic NETs, patient identification rates during the study period were 34 (89.5%) of 38 patients for MD review and 15 (39.5%) of 38 for the TR. In follow-up (performed for TR only), accounting for the effect of time lag, the TR patient identification rate would increase to 23 (60.5%) of 38 patients. Restricting the definition to that used by the TR, identifying only patients with clearly malignant disease, patient identification rates were 22 (84.6%) of 26 patients for MD review and 15 (57.7%) of 26 for the TR during the study period. Again adding those patients affected by time lag for the TR, the patient identification rate would increase to 23 (88.5%) of 26 patients; however, this does not take into account additional patients that would likely be identified by MD review during this time, because there is a constant TR time lag.

The findings of this study were presented to our institutional cancer committee in January 2010. As a result, all pancreatic NETs will now be included in our TR, even those coded as benign or defined as tumors or neoplasms. However, because of reportability standards, only those patients with unequivocally malignant disease, as defined by ICD-O-3 coding, will continue to be reported to the state TR and NCDB.

Discussion

This analysis of a single-institution academic TR shows that identification of a substantial proportion of patients with pan-

Table 1. Patient Demographics and Tumor Characteristics for All Identified Pancreatic NET Cases

Characteristic	Overall		MD Review		Tumor Registry	
	No.	%	No.	%	No.	%
No. of patients	38	100	34	89.5	15	39.4
Median age at diagnosis, years	58.2		58.6		59.1	
Sex						
Male	19	50.0	18	53.0	5	33.3
Female	19	50.0	16	47.0	10	66.7
Location of tumor						
Head	18	47.4	15	44.1	10	66.7
Body	8	21	6	17.7	4	26.7
Tail	6	15.8	7	20.6	1	6.7
Nonspecified	1	2.7	1	3	0	0
Multifocal	4	10.5	4	11.8	0	0
Neck	1	2.7	1	3	0	0
WHO classification (2004)						
Well-differentiated NET						
Benign	5	13.1	5	14.7	1	6.7
Low-grade malignant	10	26.3	10	29.4	2	13.3
Well-differentiated NE carcinoma	13	34.2	12	35.3	7	46.7
Poorly differentiated NE carcinoma	8	21.0	5	14.7	5	33.3
Unclassifiable	2	5.3	2	5.9	0	0
Nonfunctioning	28	73.7	25	73.5	13	86.7
Functioning	10	26.3	9	26.5	2	13.3
Insulinoma	2	5.3	2	5.9	0	0
Gastrinoma	5	13.1	4	10.5	2	13.3
Glucagonoma	2	5.3	2	5.9	0	0
VIPoma	1	2.7	1	2.9	0	0
Somatostatin	0		0	0	0	0

Abbreviations: NET, neuroendocrine tumor; MD review, physician medical record review; NE, neuroendocrine.

Table 2. Patients Identified by Physician Review Who Were Not Identified by Tumor Registry

Characteristic	Unidentified Patients	
	No.	%
Total	23	100
Time lag (added to tumor registry after study time period)	8	34.8
Benign per coding standards	12	52.2
True malignant, not identified (added to tumor registry because of study findings)	3	13.0

creatic NETs is not congruent with that by MD review. Our results demonstrate that the identification rate of pancreatic NETs by a single physician reviewer is more than double the identification rate of our TR (89.5% *v* 39.5%). Part of this discrepancy (21.6% of total) can be accounted for by the 6.3-month time lag associated with the TR in entering, completing,

and closing patient cases into the registry. Three patients (7.9% of total) were recognized as missed patients by the TR and were subsequently added to the database. However, the biggest discrepancy was found in the 12 patients (31.6% of total) that the TR is required to code as benign on the basis of ICD-O-3 coding, as dictated by the NAACCR reportability standards.

To our knowledge, this is the first study analyzing the accuracy of a TR in capturing pancreatic NETs. However, there have been a number of publications involving other tumor types, including primary intracranial tumors, chronic lymphocytic leukemia, non-Hodgkin's lymphoma, and colorectal, ovarian, and breast cancers, with varying degrees of accuracy.^{11,15-23} Several studies have been published about the prognosis and classification of pancreatic NETs.^{1-4,10} These studies have drawn conclusions about epidemiologic features and tumor and patient characteristics, supported by data from the NCDB.^{1-4,10} However, these studies did not review the accuracy of TR identification of pancreatic NETs.

On the basis of the present study, in using TR data, either institutional or national (eg, NCDB), 32% of the total number of patients with these rare tumors may be patients whose disease a physician would diagnose and treat as malignant; however, a TR may not capture these same patients because of a benign ICD-O-3 code. Because of the natural history of pancreatic NETs being protracted, with tumors that can metastasize or become locally invasive after months to years if left untreated,^{5,7} data published to date may be biased and may undercapture pancreatic NETs that later go on to be malignant but are assessed as not clearly malignant on initial pathology. We encouraged our TR and cancer committee to include these missing tumors in the database so that future institutional studies performed based on our TR would take into account a more accurate analysis of pancreatic NETs. However, this does not address the larger system-wide concern that the histologic WHO ICD-O-3 and medical record ICD-9 coding systems currently used to classify pancreatic NETs as benign or malignant may not be congruent with each other or, moreover, with a physician's interpretation. Thus, tumors are listed as benign that might otherwise be treated as malignant by a physician. State cancer registries and the NCDB do not, and will not, collect these patient cases until these coding rules are changed. Therefore, researchers should be aware of the limitations of TR data in describing the incidence of pancreatic NET cases.

Our study is limited by being a single-institution study of a relatively rare type of tumor; therefore, our patient numbers and power are limited. Furthermore, the natural history and histologic features of these types of tumors make them particularly difficult to classify within a TR that intends to capture only malignant cases. This perceived underreporting of patients when compared with that by physician reviewers seems largely based on different definitions of malignancy as well as different coding systems (ICD-O-3 *v* ICD-9) between TR reporting standards and the physicians. Because this difference in definitions is particularly poignant in the case of pancreatic NETs, this perceived underreporting may not be generalizable to all types of malignancy captured by TRs. Another limitation is the

inherent need for the initial screening processes for both the MD review and the TR to be based on electronic scanning systems; those patients not identified by computer processing would not be able to be further reviewed by either the physician reviewer or the TR, therefore limiting the final analyses of accuracy because true missed counts are unknown. Finally, the use of retrospective data from electronic and paper medical records may not be as accurate and complete as when data are collected prospectively.

Despite these limitations, our data clearly reflect a significant difference in the identification of pancreatic NETs by physician reviewer compared with a TR. As more studies incorporate institutional TR data, these data contribute to advances in clinical knowledge of the epidemiology and natural history of many types of tumors. This knowledge may therefore influence treatment recommendations, especially for rare or difficult-to-diagnose tumors for which aggregate data are needed. Current TR data must be analyzed in this context.

Future work should advocate for updated coding system rules, with uniform definitions and data recording systems across all centers, which would allow all TRs to most accurately identify and collect tumor cases in accordance with the scientific progress that has been made in the understanding of the pancreatic NET disease process. Where histology is stated to be uncertain, often a physician may err on the side of caution, treating a patient with a vague tumor diagnosis as having malignant potential, as is the case with most pancreatic NETs. For the same case of uncertain histology, the reporting standards applied to a TR allow collection of only truly malignant cancers as defined by WHO ICD-O-3 codes. It is recognized that in these instances, many tumors that are initially identified as benign by these codes still have malignant potential, as demonstrated with at least one patient in our study population. Therefore, further collaboration between clinicians, pathologists, and tumor registrars must be undertaken to more properly align these goals and advocate for a more unified and updated approach to the coding system. Such work may have additional policy implications for other institutional TRs. Future work should also analyze any impact on the NCDB. Using the example of our institution, all patients with pancreatic NETs will now be captured within our center, but the state and NCDB reporting will still only include those defined by ICD-O-3 codes to be malignant at time of diagnosis. Therefore, there remains a possibility for undercapturing these patient cases in state and national databases.

Analysis of an academic TR shows that a substantial proportion of the identification of patients with pancreatic NETs is

not congruent with that by MD review. Most instances of unidentified patients by TRs are the result of difficulty in precisely defining malignancy by histology, to a lesser degree of registration time lag, and rarely to truly missed cases. This may be applicable to other individual TRs as well as aggregate registry-based national studies, such as those using the NCDB. The ultimate goal of future work in this area should be in defining coding standards that allow TR, and therefore NCDB, data to reflect the best and most accurate collection of tumor cases so that these data sources are more effective for cancer research as well as development of cancer care.

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