Concordance Between ICD-10 Codes and Clinical Diagnosis of Hypoparathyroidism in Sweden

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Introduction: Chronic hypoparathyroidism is a rare disorder. The disease is characterized by low serum calcium, high serum phosphate, and deficient production of parathyroid hormone. The most common etiology is unintentional damage and intentional removal to the parathyroid glands during anterior neck surgery. Other causes include genetic disorders and autoimmune diseases. Knowledge about the epidemiology of chronic hypoparathyroidism is sparse and the prevalence in Sweden is unknown. It is of importance to know the validity of the registers used to study the epidemiology of hypoparathyroidism in Sweden.

The purpose of this study was to validate the International Classification of Diseases - 10th revision (ICD-10) diagnosis of hypoparathyroidism in the Swedish National Patient Register.

Methods: We included patients with the ICD-10 diagnosis of hypoparathyroidism that were found in the Swedish National Patient Register during 2004 to 2016. Through the unique national registration number assigned to all Swedish inhabitants, we could link this information to the Swedish Prescribed Drug Register. We included patients with an ICD-10 diagnosis for hypoparathyroidism and on concurrent conventional treatment for the disease. The validation of the diagnosis was assessed through review of medical records of 120 patients.

Results: A total of 958 patients, 70% women (n=671) and 30% men (n=287) met the inclusion criteria. In total, 120 randomly chosen medical records were reviewed and 109 cases were confirmed. This corresponds to an overall positive predictive value of 91%.

Conclusion: The validity of the ICD-10 diagnosis of hypoparathyroidism in the Swedish National Patient Register is high and the register is a reliable source for further research. There is a risk of miscoding when assigning an ICD-code to the medical records. We urge clinicians to be aware of this risk, especially the risk of mix-ups with the more common diagnosis of hyperparathyroidism.

Keywords: hypoparathyroidism, parathyroid glands, validations studies, Sweden, International Classification of Diseases, registers

Introduction

Chronic hypoparathyroidism is a rare disorder of mineral metabolism due to deficient production of parathyroid hormone.1 It is characterized by low serum calcium and high serum phosphate.2 The estimated prevalence of hypoparathyroidism range between 102 per million inhabitants in Norway, 254 in Denmark and 250 in USA per million inhabitants.2–5 Cianferotti et al found a prevalence of 270 per million inhabitants in the region of Tuscany in Italy during 2009–2013, whereas Cipriani found 530 per million inhabitants when expanding the study period from 2006 to 2013.6,7 The prevalence in Sweden is unknown. Anterior neck surgery, most commonly due to thyroid disorders, is the most common cause of hypoparathyroidism in adults, responsible for about 75% of the cases.8 Other etiologies include genetic disorders,9 autoimmune diseases,10 and infiltrative disorders such as...
metastases and iron or copper overload.¹¹ The clinical presentation of hypoparathyroidism varies from potentially life-threatening acute hypocalcemic crisis to milder symptoms of chronic hypocalcemia and hyperphosphatemia.¹¹ In the case of acute hypocalcemia, patients can present with symptoms such as seizures, cardiac rhythm disturbances, congestive heart failure, bronchospasm, or laryngospasm.¹² More commonly, patients present with symptoms due to mild hypocalcemia, such as muscle cramps and paresthesia in the extremities, but also mental disturbances often referred to as “brain fog”.¹³ Conventional therapy for chronic hypoparathyroidism includes oral calcium and active vitamin D, as well as thiazide diuretics and magnesium supplementation if needed.¹⁴

There are other diagnoses that can cause similar laboratory values as seen in hypoparathyroidism,¹⁵ for example, kidney failure, malabsorption, and hypomagnesemia.¹⁵ These conditions can also present with hypocalcemia but are characterized by high, or extremely high PTH levels. These diagnoses, as well as hyperparathyroidism, which is much more common than hypoparathyroidism, can be miscoded as hypoparathyroidism. Furthermore, registration of transient cases of hypoparathyroidism as chronic can be a cause of misdiagnosis. Most post-surgical cases of hypoparathyroidism are transient and recover within 6 months and thus should not be registered as chronic hypoparathyroidism.¹⁶ Thus, the accuracy of the diagnosis of hypoparathyroidism may be compromised for a number of reasons.

However, the accuracy of the ICD-10 of hypoparathyroidism in inpatient and outpatient care in the Swedish National Patient Register is of importance when conducting epidemiological studies based on register information. A previous review of 132 validation studies evaluating a broad spectrum of adult and pediatric disorders, including surgical, medical, and psychiatric diagnoses conducted in the Swedish Patient Register, found that the positive predictive value of the diagnoses in the inpatient register was between 85% and 95%.¹⁷ There are, as far as we know, no previous publication on the validity of the ICD-10 diagnosis of hypoparathyroidism in a national patient register.

Methods

The Registries

The Swedish National Patient Register is a population-based register covering inpatient records since 1964 and outpatient records since 2001.¹⁷ The register was founded by the National Board of Health and Welfare, a government agency.¹⁷ Sweden has universal health care and it is mandatory for all medical facilities, irrespectively to their source of funding, to report to the Swedish National Patient Register.¹⁷ The Swedish national health registries rely on the national registration number that is assigned to all Swedish Residents since 1947.¹⁸ The number is unique to each individual and consists of the person’s date of birth, a three-digit number, and a check digit.¹⁸ The check digit is computed by an algorithm and constitutes a control digit used for error detection.¹⁸ This enables merging of information between national population registries. The registers are non-anonymous in the sense that the patients are entered with their unique national registration number in the registers. When extracting information from the registers, the patients’ national registration number is replaced by a serial number. Statistics Sweden holds the key to the link between the serial number in the specific data set and the patients’ national registration number.

The Swedish Prescribed Drug Register has gathered data since July 2005 on all drugs dispensed by prescription, including quantity, dosage, expenditure, and reimbursement.¹⁹ The drug register does not, however, include information about drugs sold over the counter or for use during hospital care, nor does it hold clinical information on diagnosis or indication for treatment.²⁰ All drugs are classified according to the Anatomical Therapeutic Chemical (ATC) classification system.²⁰

We chose to conduct our study during 2004–2016. Since the Swedish Prescribed Drug Register started in 2005, we could include cases diagnosed in 2004 that were dispensed prescriptions in 2005. We were able to collect comprehensive data from all the registries until the end of 2016.

Participants

By merging data from the population-based registers above, we were able to identify a cohort of patients with a diagnosis of hypoparathyroidism on conventional treatment (Figure 1). As a first step, we included all patients that were found in the Swedish National Patient Register during 2004 to 2016, with the following ICD-10 codes for hypoparathyroidism: E20.0: Idiopathic hypoparathyroidism, E20.1: Pseudohypoparathyroidism, E20.8: Other specified hypoparathyroidism, E20.9: Hypoparathyroidism unspecified, E89.2: Postprocedural hypoparathyroidism, D82.1: DiGeorge syndrome, and E31.0: Autoimmune polyglandular failure. Hypoparathyroidism of all causes was included, including autosomal dominant hypocalcemia and hypoparathyroidism due to ineffective PTH-action. As a second
step, we used the national registration numbers to link information from the Swedish National Patient Register to information in the Swedish Prescribed Drug Register. To decrease the risk of including patients with transient post-surgical hypoparathyroidism, we only included patients who received at least three prescriptions of conventional treatment with calcium and active vitamin D during the first year of inclusion or two prescriptions per year during two consecutive years after the inclusion in the Swedish National Patient Register (Table 1).

We excluded patients with the following ICD-10 codes: E83.5: Disorders of calcium metabolism, E21.4: Other specified disorders of parathyroid gland, and E31.8: Other polyglandular dysfunction, since these diagnoses are unspecific and some can include disorders of both hypo- and hypercalcemia.

Outcome Measures
We validated the diagnosis of hypoparathyroidism through review of medical charts. We aimed to review 10% of the estimated cases in Sweden and we added an extra 2% to allow for loss to follow-up. This estimation was based on the prevalence of hypoparathyroidism in Norway reported by Astor et al.² To get a sample representing both cities and the countryside, we randomly chose three counties (Stockholm, Uppsala, and Linköping) which had both a university hospital and at least one regional hospital.

In total 120 medical charts were reviewed by three specialists in endocrinology that either confirmed or repudiated the diagnosis according to a pre-specified protocol. In case of ambiguity, the reviewers could discuss with each other. We calculated the positive predictive value by dividing the true cases in the Swedish National Patient Register with all the cases (true and false) that were reviewed.

This study was approved of the Stockholm County Regional Ethics Review Board (reference number 2017/476-31/4).

Results
In total 958 patients fulfilled the inclusion criteria of having a diagnosis of hypoparathyroidism and being on

| Table 1 Drug Groups of Conventional Treatment of Hypoparathyroidism in Sweden 2004–2016 (n=958) |
| Drug Groups | Patients (n) |
|-------------|--------------|
| Drug group 1: Calcium with/without vitamin D and active vitamin D | 951 |
| Drug group 2: Calcium with/without vitamin D and active vitamin D and Teriparatide | 2 |
| Drug group 3: Calcium with/without vitamin D and Teriparatide | 3 |
| Drug group 4: Calcium with vitamin D | 23 |

Notes: Seventeen patients received drugs from drug groups 1 and 4. Two patients received drugs from drug groups 1, 2, and 3.
conventional treatment (Figure 1). Of those were 70% women (n=671) and 30% men (n=287).

The most common treatment was a combination of calcium and active vitamin D, with or without native vitamin D, which was the case in 99% of the included patients. Few patients (n=3) were treated with Teriparatide (Table 1). Post-surgical hypoparathyroidism was the most common cause of hypoparathyroidism (n=664) (Table 2).

The hypoparathyroidism diagnosis was confirmed as correct in 109 out of the 120 randomly selected cases, resulting in a positive predictive value of 91%. In 11 cases, a misclassification of the diagnosis was found. Out of the misclassified cases, four had kidney failure, one case had kidney transplantation, five had hyperparathyroidism, and one had hypothyroidism.

Discussion
In this study of almost 1000 patients with a diagnosis of, and treatment for hypoparathyroidism, we found hypoparathyroidism to be more common in women than men, and the most common cause of hypoparathyroidism to be anterior neck surgery, which is in line with previous epidemiological data.\(^1\)\(^-\)\(^3\) The vast majority of patients were treated with a combination of calcium and active vitamin D – which is according to the European guidelines.\(^16\) However, treatment with Teriparatide was extremely rare. This type of treatment with the deficient hormone is appealing, and Sikjaer et al showed that the dosage of calcium and vitamin D could be reduced during treatment.\(^21\) Nonetheless, teriparatide is not yet recommended as an add-on treatment, which is demonstrated in our study.

In our review of 120 medical charts, we found a high positive predictive value for the diagnosis of hypoparathyroidism. This is consistent with previous research of other ICD-diagnoses in the Swedish National Patient Register.\(^17\) The Swedish National Patient Register is thus a reliable source for conducting nationwide epidemiological studies on hypoparathyroidism.

Sweden has a government-sponsored healthcare system where all prescribed drugs are subsidized. One of the strengths of this study is that our cohort was selected, not only based on the ICD-10 diagnosis in the patient register but also filtered by the relevant treatment for hypoparathyroidism in the Swedish Prescribed Drug Register. This increased the accuracy and permitted us to make the distinction between transient and true chronic hypoparathyroidism of all causes.

We do not believe that excluding patients with pseudo-hypoparathyroidism would have changed the results since this is an unusual diagnosis. However, using our strict criteria may have resulted in an underestimation of the diagnosis of chronic hypoparathyroidism. For example, patients with mild hypoparathyroidism could potentially be treated with calcium over the counter without a medical prescription. However, the calcium concentration for over the counter calcium is only 120 mg/tablet. Additionally, the government only subsidizes prescribed drugs. We, therefore, believe it is highly unlikely that patients would choose this low-dose, more expensive, over the counter option.

A larger sample size in our study may have improved the PPV, nonetheless, by using two high-quality population-based registers to include our patients we increased the precision of the data. The reliability of the Swedish National Patient Register can further be improved by increasing awareness amongst clinicians regarding the risk for misclassification of the ICD-diagnosis. Clinicians treating patients with hypocalcemia need to consider if the patient has an underlying kidney failure before making a decision on the most appropriate diagnosis. It is also of importance to be aware that it is possible to confuse “hyper-“ and “hypo-“ when the diagnosis of hypoparathyroidism is assigned in the medical records. This is important to bear in mind as the diagnosis of hyperparathyroidism is more common than hypoparathyroidism.\(^22\)

To conclude, hypoparathyroidism was most frequently seen in women, and after anterior neck surgery. The validity of the ICD-10 diagnosis of hypoparathyroidism in the Swedish National Patient Register is high. There is a risk of miscoding when assigning an ICD-code to the medical records, where we urge clinicians to be careful, not to confuse hypoparathyroidism with hyperparathyroidism or hypocalcemia due to kidney disease.

Table 2 Diagnostic Groups According to ICD-10 Code in the Swedish National Patient Register 2004–2016

| ICD-10 Code - Diagnostic Groups | Total |
|--------------------------------|-------|
| E20.0: Idiopathic hypoparathyroidism | 118   |
| E20.1: Pseudohypoparathyroidism | 26    |
| E20.8: Other specified hypoparathyroidism | 73    |
| E20.9: Hypoparathyroidism unspecified | 223   |
| E89.2: Postprocedural hypoparathyroidism | 664   |
| D82.1: DiGeorge syndrome | 10    |
| E31.0: Autoimmune polyglandular failure | 3     |

Notes: Nine hundred and fifty-eight cases had in total 1117 diagnoses for hypoparathyroidism during the study period.
Disclosure
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