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Hospital discharge diagnoses of ventricular arrhythmias and cardiac arrest were useful for epidemiologic research

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Abstract

Objective: We investigated the validity of hospital discharge diagnosis regarding ventricular arrhythmias and cardiac arrest.

Methods: We identified patients whose record in the PHARMO record linkage system database showed a code for ventricular or unspecified cardiac arrhythmias according to codes of the International Classification of Diseases, 9th revision, clinical modification (ICD-9-CM). The validity of ICD codes for ventricular arrhythmias and cardiac arrest (427.1, 427.4, 427.41, 427.42, 427.5, 427.69) and ICD codes for unspecified cardiac arrhythmias (427.2, 427.60, 427.8, 427.89, 427.9) was ascertained through manual review of hospital clinical records. The positive predictive value (PPV) was calculated, and differences between characteristics of true and false positives were evaluated.

Results: The PPV of ICD codes for ventricular arrhythmias and cardiac arrest was 82% (95% confidence interval CI = 72–92). True positive results were associated with male gender ($P = .09$) and younger age ($P = .05$). Of the unspecified cardiac arrhythmias 10% (95% CI = 2–18) were identified as ventricular arrhythmias or cardiac arrest.

Conclusion: Hospitalizations for ventricular cardiac arrhythmias and cardiac arrest (coded according to ICD-9-CM as paroxysmal ventricular tachycardia, ventricular fibrillation, ventricular flutter, ventricular premature beats, or cardiac arrest) have a high PPV and are useful for selecting events in epidemiological studies on drug-induced arrhythmias.

Keywords: Patient discharge; Predictive value of tests; Ventricular arrhythmia; Cardiac arrest

1. Introduction

Adverse drug reactions that require hospitalization fulfill the criteria for *serious* according to the ICH Harmonised Tripartite Guideline [1]. Hospitalizations are widely used to define outcomes in pharmacoepidemiologic database studies on side effects of drugs [2–6]. The most commonly used coding system to categorize hospital discharge diagnosis is the International Classification of Diseases (ICD) [7]. Classification in a computerized medical database can be subject to errors, however, ranging from incomplete reporting by a physician to typing errors by a coding clerk [8]. Several researchers have assessed the validity of hospital discharge records for various diseases, comparing the data with either original medical records [9–12] or computerized information from the clinical chemical laboratory [13].

Drugs that prolong cardiac repolarization, manifested as a prolonged QTc interval on the surface electrocardiogram (ECG), may induce torsade de pointes ventricular tachycardia, which is generally preceded by ventricular premature beats [14]. Torsade de pointes may develop into ventricular fibrillation, which leads to cardiac arrest and requires electrocardioversion to restore normal rhythm [15]. Hospitalizations for ventricular arrhythmias and cardiac arrest may function as an epidemiologic study endpoint of interest, when assessing the risk for drug-induced arrhythmias among patients taking QTc-prolonging drugs.

We investigated the positive predictive value (PPV) of hospital discharge diagnosis of ventricular cardiac arrhythmias and cardiac arrest, classified according to ICD codes

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matching this definition. In addition, ICD codes for unspecified cardiac arrhythmias were scrutinized for ventricular cardiac arrhythmias and cardiac arrest as well.

2. Methods

2.1. Setting

Data were obtained from the PHARMO record linkage system, which contains drug dispensing records from community pharmacies and linked hospital discharge records of a defined population of 330,000 residents of eight medium-sized Dutch cities. In the Netherlands, as in many other countries, every hospital must to collect diagnostic data on all admissions. Discharge diagnoses, coded according to the International Classification of Diseases, 9th revision, clinical modification (ICD-9-CM), are obtained from the discharge abstract form (retrieved from the medical record). At discharge, treating physicians are asked to fill in the principal diagnosis (primary hospital discharge diagnosis) that precipitated the hospital admission on these forms. The source population of the present study consists of all hospital diagnostic records from four randomly picked hospitals in the PHARMO area between 1999 and 2000, regardless of whether patients were taking medication at that time.

2.2. Case definition

Cases were defined as incident primary hospital discharge diagnoses for ventricular or unspecified cardiac arrhythmias. If patients experienced multiple events during the study period, only the first event was used.

When studying drug-induced arrhythmias the study endpoint of interest is ventricular arrhythmias and cardiac arrest. ICD codes that match this study endpoint include paroxysmal ventricular tachycardia (427.1), ventricular fibrillation and/or flutter (427.4, 427.41, 427.42), cardiac arrest (427.5), and ventricular premature beats (427.69). These ICD codes were used to calculate the positive predictive value (PPV). Other (unspecified) cardiac arrhythmias, which may also include ventricular arrhythmias and cardiac arrest, were studied as well, to get an estimation of the sensitivity of the specific diagnoses for ventricular arrhythmias and cardiac arrest. These broader definitions included ICD codes for paroxysmal tachycardia, unspecified (427.2), premature beats, unspecified (427.60), other cardiac dysrhythmias (427.8, 427.89), and cardiac dysrhythmias, unspecified (427.9).

2.3. Validation

Medical records of the cases were retrieved from the four hospitals and were reviewed by an independent cardiologist, blinded for the coded discharge diagnosis. Hospital discharge letter, ECGs at hospital admission and at discharge date, and serum electrolyte levels were scrutinized. When no discharge letter was available, copies from the original medical chart were provided. The cardiologist was asked to give a diagnosis based on the available data and to categorize this new diagnosis according to the ICD-9-CM. The researchers assigned the cardiologist's diagnosis to one of the following four categories:

1. Ventricular arrhythmia or cardiac arrest (ICD-9-CM 427.1, 427.4, 427.41, 427.42, 427.5, 427.69);
2. Other cardiac arrhythmia (ICD-9-CM 427.0, 427.2, 427.3, 427.31, 427.32, 427.6, 427.60, 427.61, 427.8, 427.81, 427.89, 427.9);
3. Other cardiac diagnosis, no arrhythmia (ICD-9-CM 390–426, 428–459); and
4. No cardiac diagnosis.

2.4. Data analysis

The positive predictive value (PPV) of hospital discharge diagnoses for ventricular arrhythmias and cardiac arrest was calculated as the percentage of the cases with an ICD code 427.1, 427.4, 427.41, 427.42, 427.5 or 427.69 assigned to category 1. Taking the independent cardiologist's diagnosis as the gold standard, cases assigned to category 1 were regarded as true positives, and cases assigned to categories 2, 3, and 4 were regarded as false positives. The 95% confidence intervals (95% CI) were calculated according to Altman [16]. Differences between characteristics of true and false positives were evaluated. Continuous variables and proportions were compared using the Student's *t*-test and chi-square test, respectively. Fisher's exact test was used if not all expected numbers in a two-by-two table were $\geqslant 5$.

To get an estimation of the sensitivity of the specific diagnoses for ventricular arrhythmias and cardiac arrest, we also calculated the percentage of cases with an ICD code for unspecified cardiac arrhythmias (427.2, 427.60, 427.8, 427.89, 427.9) that were assigned to category 1.

3. Results

During the study period, a total number of 111 patients were admitted to one of the four hospitals for ventricular or unspecified cardiac arrhythmias for the first time. All medical records could be retrieved and included 61 records of patients with an ICD code for ventricular arrhythmias or cardiac arrest and 50 records of patients with an ICD code for unspecified cardiac arrhythmias (Table 1). Overall, 55 of the 111 selected discharge diagnoses were validated as being either ventricular cardiac arrhythmia or cardiac arrest. Of the 61 hospitalizations with ICD codes for ventricular cardiac arrhythmia or cardiac arrest, 50 were validated as such, giving a PPV of 82% (95% CI = 72–92). All individual ICD codes within this group had a PPV of at

least 65%, and true positive results were associated with male gender ($P = .09$) and younger age ($P = .05$); no differences were found between hospitals or between year of hospitalization (Table 2). The percentage of diagnoses assigned to category 1 among the unspecified cardiac arrhythmias was as low as 10% (95% CI = 2–18), ranging from 0% to 19% according to the individual ICD codes (Table 1). This percentage was associated with hospital ($P = .04$) and year of hospitalization ($P = .05$).

Forty patients (36%) were diagnosed as having a cardiac arrhythmia outside the case-definition, being a well-defined nonventricular arrhythmia (e.g., supraventricular tachycardia) in 34 of the cases. Of two of the well-defined diagnoses, the ventricular origin could not be verified, whereas of the other diagnoses in four cases no ventricular nor other specific type of arrhythmia could be identified (Table 1). Sixteen patients (14%) were not admitted to the hospital for cardiac arrhythmias at all. Most of these patients, however, experienced cardiac arrhythmias at some time during their hospitalization, or were observed for ECG abnormalities, except for three patients: in two cases, a vasovagal collapse was misinterpreted as a cardiac arrest (427.5), and in another case a cardiac conduction disorder (AV-block) was coded as a cardiac dysrhythmia (427.89).

4. Discussion

In this study, we found a positive predictive value of 82% for ventricular arrhythmias and cardiac arrest of hospitalizations specifically coded as such according to the ICD-9-CM classification. The PPV did not depend on hospital, nor on year of hospitalization, and therefore extrapolation of the results to other hospitals and other years may be justified. Other diagnoses most likely to include some of the misclassified ventricular cardiac arrhythmias and cardiac arrest cases (ICD codes for unspecified cardiac arrhythmias) were identified only as ventricular cardiac arrhythmias or cardiac arrest in 10% of the cases, indicating a high sensitivity for the outcome of interest among the selected ICD codes (427.2, 427.60, 427.8, 427.89, 427.9).

Correct classification according to ICD codes appeared to be more difficult for women and for older patients. Female gender is related to age within these 61 patients (mean age for women was 70 years, vs. 62 for men), and age may be correlated with disease complexity, making it difficult to assign primary ICD codes. This hypothesis is supported by the fact that most of the patients that, according to our gold standard, did not meet the criteria of primary hospital discharge diagnosis of cardiac arrhythmias, did experience cardiac arrhythmia at some time during their hospitalization. Other mistakes that were made during the coding process included assigning ECG observations to ICD codes of suspected diseases which could not be verified, misinterpretation of other diseases with similar symptoms (such as vasovagal collapse) as being cardiac arrhythmias, and coding specific cardiac arrhythmias into unspecified categories, either due to misinterpretation by the coding clerk or lack of clearly described information by the treating physician.

As far as known, no previous studies on validation of the study outcome in research on drug-induced arrhythmias have been performed. Most epidemiologic studies on this side effect used quite broad outcome definitions, followed by case verification through screening of all original medical records. As expected, much lower PPVs were calculated from these studies, compared to our study. The PPV varied from 4% to 73% in studies using claims data [17–19] and from 12% to 27% in studies using data from general practices [20,21]. In a study using hospital discharge codes, cardiac outpatient encounters and sudden deaths as a combined outcome, the positive predictive value of the study outcome was 14% [20].

A factor that might have influenced our results is the fact that we were not able to use a more comprehensive medical

Table 1
Validated diagnoses of hospital discharge diagnosis for ventricular and unspecified cardiac arrhythmias as well as cardiac arrest

Observed ICD-9-CM code	VA or CA[a]	% of total	Other arrhythmia[b]	Other cardiac dx[c]	No cardiac dx	Total
Ventricular arrhythmias and cardiac arrest	50	82[d]	4	4	3	61
427.1 Paroxysmal ventricular tachycardia	24	100[d]				24
427.41 Ventricular fibrillation	10	77[d]	1	2		13
427.5 Cardiac arrest	13	65[d]	2	2	3	20
427.69 Ventricular premature beats	3	75[d]	1			4
Unspecified cardiac arrhythmias	5	10	36	4	5	50
427.2 Paroxysmal tachycardia, unspecified		0	1			1
427.60 Premature beats, unspecified		0			1	1
427.89 Other cardiac dysrhythmias	2	6	27	2	1	32
427.9 Cardiac dysrhythmias, unspecified	3	19	8	2	3	16
Total	55	50	40	8	8	111

Abbreviations: CA, cardiac arrest; dx, diagnosis; VA, ventricular arrhythmia.

[a] Ventricular arrhythmia or cardiac arrest (ICD-9-CM 427.1, 427.4, 427.41, 427.42, 427.5, 427.69).

[b] Other cardiac arrhythmia (ICD-9-CM 427.0, 427.2, 427.3, 427.31, 427.32, 427.6, 427.60, 427.61, 427.8, 427.81, 427.89, 427.9).

[c] Other cardiac diagnosis, no arrhythmia (ICD-9-CM 390–426, 428–459).

[d] Positive predictive value.

Table 2
Determinants of misclassification of hospitalizations coded as ventricular cardiac arrhythmias or cardiac arrest

	False positives, $n = 11$	True positives, $n = 50$	P-value
Gender			
Male, no. (%)	4 (11)	34 (89)	.08
Female, no. (%)	7 (30)	16 (70)	
Hospital			
A, no. (%)	5 (19)	22 (81)	.94
B, no. (%)	2 (18)	9 (82)	
C, no. (%)	1 (11)	8 (89)	
D, no. (%)	3 (21)	11 (79)	
Year			
1999, no. (%)	5 (14)	30 (86)	.50
2000, no. (%)	6 (23)	20 (77)	
Age, years, mean (SD)	71 (10)	64 (16)	.05

Abbreviations: SD, standard deviation.

history for diagnosis by the independent cardiologist. Although we think that we have used the most relevant information needed to make a diagnosis, more detailed information or contact with the physician who treated the specific patient could have improved the accuracy of the gold standard diagnosis. It is therefore possible that some residual misclassification is still present in our validated outcomes, and that true PPVs are lower than presented. Another limitation is that, although the results may be applicable to other hospitals, extrapolation outside the Netherlands may not be allowed, because of potential differences between countries in coding of hospital discharge diagnoses. In addition, coding hospital discharge diagnoses according to the latest version of ICD (ICD 10), which uses a slightly different categorization of cardiac arrhythmias than ICD 9 CM, may lead to different coding mistakes than we describe in this study.

For this study, we used primary hospital discharge diagnoses. Ventricular arrhythmias and cardiac arrest may also be coded as secondary discharge diagnoses, as when, for instance, they occurred as a result of a myocardial infarction and the infarction was the primary reason for hospitalization. Because we believe that pharmacoepidemiological studies on drug-induced arrhythmias occurring through QTc-prolongation should exclude noniatrogenic conditions as much as possible in their outcome definition, we excluded the secondary diagnoses, which are likely to be noniatrogenic [22].

Misclassification of outcome may occur in both case-control and cohort studies. In case-control studies, outcome misclassification influences the selection of cases and controls in the study. In cohort studies, it is related to the way the information on study variables is measured during the study, after index and control groups have been defined, and may cause information bias [23].

In general, selection bias in case-control studies, as a result of disease misclassification, occurs when not all observed cases (or controls) are true cases (or controls). It is therefore important to study how much of the cases (and controls) are true cases (and controls), which can be measured through positive (and negative) predictive values. In case of a rare disease, misclassification from diseased to nondiseased patients will cause a negligible decrease in negative predictive value of the controls, making the PPV of disease the most important measure in overall validity assessment.

In addition, cases which are included in a case-control study should be representative for all cases that occurred. In the case of drug-induced arrhythmias it may possible that patients have died from the cardiac arrhythmias before they were admitted to the hospital. However, the impact of this potential selective inclusion of survivors on the results of case-control studies on drug-induced arrhythmias using hospitalizations as an endpoint is beyond the scope of this present study.

In conclusion, hospitalizations for ventricular cardiac arrhythmias and cardiac arrest, coded according to ICD-9-CM as paroxysmal ventricular tachycardia, ventricular fibrillation, ventricular flutter, ventricular premature beats or cardiac arrest, have a high PPV of 82%. In addition, we have reasons to believe that the sensitivity of these codes is quite high as well. Therefore, these codes are useful for selecting events in epidemiological studies on drug-induced arrhythmias.

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