Validation of Serious Ventricular Arrhythmias in an Administrative Database

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ABSTRACT

BACKGROUND: Pharmacoepidemiology studies examining serious ventricular arrhythmias (SVA) may ascertain this outcome from data on hospitalizations, but there is limited information on the validity of these diagnoses in administrative databases. An ongoing study of SVA and sudden cardiac death (SCD) offered the opportunity to perform such a validation.

OBJECTIVE: To describe the validity of a two-stage process for identifying idiopathic SVA among hospital discharges in the Canadian Saskatchewan Health (SH) database.

METHODS: The study population comprised over 86,000 users of domperidone or a proton pump inhibitor (PPI) by prescription (1990-2005). Hospitalizations with ICD-9 and ICD-10-CA codes specific to ventricular tachycardia (VT) or ventricular fibrillation (VF) as the principal diagnosis were identified. A cardiologist, blinded to the exposure of interest, reviewed electronic patient profiles; cases with terminal illness, cancer, or other prespecified known immediate causes of arrhythmia were excluded. Suspected cases were validated by hospital medical record abstraction. The positive predictive value (PPV) was calculated for the SVA screening algorithm. Validation of non-cases was not performed.

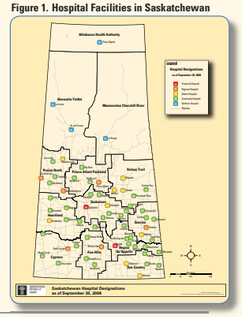
RESULTS: A total of 117 patients met the screening definition of SVA; after profile review, 74 were judged as suspected cases for abstraction. Of these, 65 records (88%) were abstracted and 34 were validated as idiopathic SVA (PPV = 52%; 95% CI: 40%-65%). An additional 14 cases were confirmed as SVA but did not meet the study criteria for idiopathic SVA. Thus, the PPV of the screening algorithm for all SVA (idiopathic or not) among the validated cases was 74% (95% CI: 63%-85%).

CONCLUSIONS: Even when using hospital discharge diagnoses, case validation is useful for identifying SVA and appears essential for identifying idiopathic SVA. Profile review before chart abstraction can increase the efficiency of the validation process.

BACKGROUND

- Evaluation of infrequent adverse events, such as drug-induced SVA, requires large populations of exposed patients.
- Population-based administrative databases are a useful resource for postmarketing safety studies, but information in administrative claims alone is often not sufficient to accurately identify outcomes such as drug-induced SVA.
- Possible SVA cases can be identified through hospital discharge diagnoses codes; however, there is limited information on the validity of these diagnoses, and additional sources of information, such as hospital records, are usually required to identify valid SVA cases.
- A validation study was performed as part of an ongoing case-control study on the risk of SVA or SCD nested in a cohort of users of domperidone or PPI medications identified from the Canadian SH database.
- We present the results of the validation process of SVA cases identified by specific hospital discharge codes.

Figure 1. Hospital Facilities in Saskatchewan



OBJECTIVE

To describe the validity of a two-stage process for identifying idiopathic SVA cases among hospital discharges in the SH database.

METHODS

Study Population

- A cohort of over 86,000 persons with at least one dispensing of domperidone or a PPI from 1990 to 2005 was identified using the SH database.
- After excluding persons with a diagnosis of cancer, the final study cohort comprised 83,212 persons.
- Follow-up time for case ascertainment began with the date of cohort entry and extended until the date of an event, death, disenrollment from the SH database, or the study end date of 12/31/2005.
- All study data were deidentified and provided by SH after review and approval of the study protocol by SH's Data Access Review Committee.

Case Ascertainment

- Suspected SVA cases were identified from hospitalizations with specific codes for VT or VF as the principal diagnosis (Table 1).
- Hospitalizations with cardiac arrest (CA) codes were screened to identify potential SVA leading to CA (Table 1).
- Chronologically recorded information in the databases was used to create electronic patient profiles.
- A cardiologist, blinded to the exposure of interest, reviewed electronic patient profiles; cases with terminal illness, cancer, or other prespecified known immediate causes of arrhythmia were excluded.
- "Suspected" SVA cases were selected for hospital record review and medical record abstraction.

Table 1. Specific Codes for SVA or CA

Diagnosis	ICD-9	ICD-10-CA
SVA	427.1, 427.4	I47.0, I47.2, I49.00, I49.01
CA	427.5	I46.0, I46.1, I46.9

ICD-9 = International Classification of Diseases, 9th Revision; ICD-10-CA = International Classification of Diseases, 10th Revision, Canadian Enhancement.

Case Verification

Abstraction Process

- An abstraction form was developed and submitted with the study protocol to the University of Saskatchewan Biomedical Research Ethics Board for review and approval.
- SH contacted the regional health authorities for permission to abstract charts and executed contract agreements with 10 regional health authorities and 6 affiliated facilities for access to hospital records.
- The abstractions were performed by SH health workers after completing a full day of in-person training conducted by RTI Health Solutions project staff.
- Records were abstracted on-site at facilities, and supporting materials (e.g., discharge summaries, electrocardiograms) were deidentified and copied.
- Materials were sent to RTI-HS after all information on the drug exposures of interest were masked.

Case Validation

- Before reviewing suspected cases, written criteria were established for case validation, following recommended criteria summarized in international clinical guidelines issued jointly by the American College of Cardiology, the American Heart Association, and the European Society of Cardiology for management of patients with ventricular arrhythmias and the prevention of SCD.[1]
- Based on all the available information, the cardiologist classified each reviewed case into one of the following categories for SVA:
  - Definite
  - Probable
  - Possible
  - Noncase.
- The data evaluated for this classification included:
  - Clinical symptoms at presentation
  - Copies of ambulance emergency services
  - Copies of electrocardiograms
  - Copies of discharge reports
  - Abstracted clinical information, including laboratory values
  - Other tests results, as available.
- This validation process was performed without knowledge of the exposure status of interest. No validation was performed on non-SVA suspected cases.

Table 2. Case Definition

Serious Ventricular Arrhythmia			
Definition	First diagnosis of a fatal or nonfatal VA with hospitalization or confirmed by a specialist during the study period		
Idiopathic SVA	SVA as defined above and no prespecified alternative cause was documented immediately before or concurrently with the SVA occurrence in the same hospitalization episode in the hospital medical record		
Diagnoses	TdP, VT, VF		
Prespecified alternative causes [a]	• Acute coronary syndrome or myocardial infarction (within 7 days) • Pulmonary arterial hypertension or acute pulmonary embolism • Chronic coronary heart disease with presence of clinical heart failure leading to VA	• Cardiomyopathy (dilated, hypertrophic, arrhythmogenic right ventricular) or congenital heart disease • Chronic coronary heart disease with presence of clinical heart failure leading to VA • Acute stroke or cerebrovascular disease	• Aortic aneurysm dissection • Valvular heart disease • Cardioverter defibrillator implanted • Terminal illness, as manifested by, for example, coma or shock
Cardiac Arrest			
Definition	Unexpected circulatory arrest, usually due to a cardiac arrhythmia, occurring within 1 hour of the onset of symptoms, in which medical intervention (e.g., defibrillation) reversed the event		
Diagnoses	• VT, TdP, or VF leading to the CA hospitalization, and • CA not precipitated by another mechanism, such as complete atrioventricular block, other type of arrhythmia, severe bradycardia, or terminal illness		
Prespecified alternative causes [a]	• Same as above plus serious respiratory compromise occurring immediately before or concurrently with a CA		

TdP = torsades de pointes; VA = ventricular arrhythmia.

[a] The presence of potential triggering factors for SVA, such serum electrolytic disturbances, dialysis, abuse of recreational drugs, or pacemaker inserted, were not considered as alternative causes.

PPV

- The PPV was calculated for the SVA screening algorithm as the number of confirmed cases among the total number of hospital charts abstracted with specific primary discharge codes for VF or VT.
- The PPV for confirmation of study cases for the CA screening also was calculated.

RESULTS

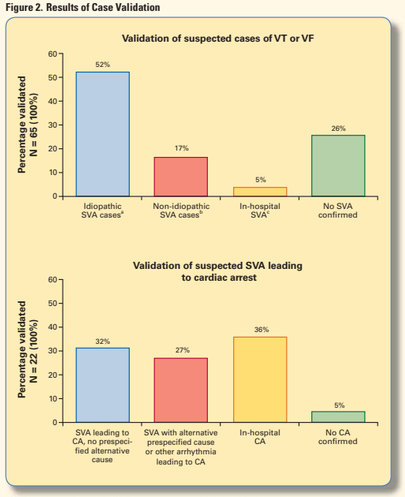
- A total of 117 patients met the screening definition of SVA (Table 3).
- After the review of the electronic patient profiles by a cardiologist and after excluding those patients with malignant neoplasm, 74 patients were judged as suspected cases for abstraction.
- Of these, nine charts were not abstracted because the chart was in an out-of-reach facility or had been destroyed.
- Completed abstractions were achieved for 65 suspected cases (88%).
- In addition, 22 suspected CA cases were abstracted.

Table 3. Subjects Selected for Electronic Patient Profile Review and Recommended for Medical Record Abstraction

Hospital Primary Discharge Code		Diagnoses SVA	Algorithm Suspected	Recommended for Abstraction
ICD-9	ICD-10-CA		N	N
427.1, 427.4	I47.0, I47.2, I49.0	VT, VF	117 (100%)	74 (63%)
427.5	I46.0, I46.1, I46.9	CA	138 (100%)	30 (22%)

- Overall, 34 cases were confirmed as idiopathic SVA according to the prespecified criteria (Figure 2).
- An additional 14 cases were confirmed as SVA but did not meet the study criteria for idiopathic SVA. In three of these nonstudy cases, the SVA occurred in the hospital.
- Among suspected CA cases, seven were confirmed as SVA leading to the arrest and without prespecified alternative cause.
- In 14 cases the CA had an alternative cause or was due to other type of arrhythmia. Of note is that 36% of suspected CA cases occurred in the hospital.

Figure 2. Results of Case Validation



[a] Confirmed case of idiopathic SVA: includes cases validated as definite, probable, and possible.

[b] Nonidiopathic SVA cases: SVA was confirmed but did not meet the study case definition because there was clear evidence of a prespecified alternative cause.

[c] In-hospital cases: Diagnosis was confirmed as SVA or CA, but the onset of the event was during a hospitalization episode (in-hospital events).

Table 4. PPV of Screening Criteria for the Confirmation of Cases of SVA and CA Fulfilling the Study Case Definition

Screening by Primary Hospital Discharge Codes	Diagnoses	PPV Formula	PPV of Confirmed Idiopathic SVA	95% CI
VT, VF	Idiopathic SVA	34 of 65	52%	40%-65%
	All SVA	48 of 65	74%	63%-85%
CA	SVA leading to CA, without prespecified alternative cause	7 of 22	32%	15%-53%

CONCLUSIONS

- Information from electronic administrative health databases, even when using hospital discharge diagnosis codes specific to SVA and after the review of detailed patient's chronological information, may be insufficient for establishing an accurate diagnosis of SVA.
- For drug safety studies with SVA as an endpoint, case validation is useful for identifying SVA cases and appears essential for identifying idiopathic SVA.
- Validation of CA hospitalizations is essential for identifying SVA as the leading cause and specifically when the outcome definition excludes in-hospital events.
- Profile review before chart abstraction can increase the efficiency of the validation process.

REFERENCES

1. Zipes DP, Camm AJ, Borggrefe M, Buxton AE, Chaitman B, Fromer M, et al. ACC/AHA/ESC 2006 guidelines for management of patients with ventricular arrhythmias and the prevention of sudden cardiac death: a report of the American College of Cardiology/American Heart Association Task Force and the European Society of Cardiology Committee for Practice Guidelines (Writing Committee to Develop Guidelines for Management of Patients with Ventricular Arrhythmias and the Prevention of Sudden Cardiac Death). Circulation 2006;114:e385-e484.

CONFLICT OF INTEREST STATEMENT

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Disclaimer: This study is based, in part, on deidentified data provided by the Saskatchewan Ministry of Health. The interpretation and conclusions contained herein do not necessarily represent those of the government of Saskatchewan or the Saskatchewan Ministry of Health.

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