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Ascertainment of warfarin and aspirin use by medical record review compared with automated pharmacy data

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Abstract

Purpose—Automated pharmacy databases are increasingly available for assessing medication use, but research on the validity of these data is incomplete. This study aimed to measure agreement on warfarin and aspirin use between medical records and automated pharmacy data among patients with newly detected atrial fibrillation (AF).

Methods—Patients with newly detected AF ($n = 1953$) were previously identified in a cohort study at Group Health (GH) in Washington State. Medical records were reviewed for information on risk factors and medication use, as well as clinical care during the 6 months after AF onset. Medication data were also obtained from the GH pharmacy database. We determined the sensitivity, specificity, and positive predictive value (PPV) as measures of the validity of the GH pharmacy database as compared with medical records for warfarin and aspirin use during the first 6 and 3 months after AF onset. We also calculated the κ statistic.

Results—For warfarin use, in comparison with the medical record review, the sensitivity, specificity, and PPV for the GH pharmacy database were excellent, and agreement was almost perfect in the 3- and 6-month periods after AF onset ($\kappa = 0.92$ and 0.93 , respectively). For aspirin use, the GH pharmacy database had low sensitivity but high specificity, and agreement was only fair for these two periods ($\kappa = 0.28$ and 0.31 , respectively).

Conclusions—The GH pharmacy database is a valuable source of data for pharmacoepidemiologic research on warfarin use among patients with AF. However, the database cannot be recommended for assessment of aspirin use.

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CONFLICT OF INTEREST

All of the authors declare no financial, personal, commercial, or academic conflicts of interest, and none related to study interpretation. Additionally, the study sponsors had no involvement in the study design, in the data collection, analysis and interpretation, in the writing of the report, or in the decision to submit the report for publication.

Keywords

warfarin; medical records; pharmacy database; pharmacoepidemiology; validity; agreement

INTRODUCTION

Atrial fibrillation (AF) is a cardiac arrhythmia which can lead to clot formation in the cardiac atria and subsequent stroke. Antithrombotic therapy is recommended for patients with AF based on their risk for thromboembolism. In the US, warfarin and aspirin are the most commonly prescribed antithrombotic agents, with warfarin used in moderate to high-risk patients.¹

Accurate assessment of warfarin and aspirin use is important in studying the association of AF with embolic risk and other health outcomes. Comprehensive prescription medication data may be best obtained through medical record review, but collecting these data can require substantial time and resources. Self-reported information is often the primary source of medication data although inaccurate recall can limit its usefulness.² Automated pharmacy databases are increasingly available, but research on the validity of these data is incomplete.^{2,3} We used data from an observational study of patients with newly detected AF to assess agreement on warfarin and aspirin use between medical records and automated pharmacy data.

METHODS

The data for these analyses came from a cohort study designed to analyze thrombotic risk and other complications in patients with newly detected AF at Group Health (GH), a large integrated health-care delivery system in Washington State.⁴ The GH Human Subjects Review Committee approved study procedures. Waiver of consent was granted for patients with language or cognitive difficulty and for patients who had died. All other participants provided written consent or verbal consent by telephone.

We identified all GH enrollees aged 30–84 years who had been assigned an International Classification of Diseases, Ninth Revision (ICD-9) code for AF (427.31, AF; or 427.32, atrial flutter) during any inpatient or outpatient visit between 1 October 2001 and 31 December 2004, and who had never before been assigned an AF ICD-9 code during their GH enrollment.^{4,5} Medical records were reviewed to verify the diagnosis of newly detected AF and to collect information on risk factors and medication use, both before and after AF onset. There were 1953 eligible cases of newly detected AF.

The GH ambulatory medical record includes notes from primary care and specialty physician visits, emergency department visit notes, discharge summaries from hospitalizations, consultant reports, information from telephone contacts, and laboratory and diagnostic test reports. Blood pressure levels and weights are routinely recorded and active problem lists are maintained. Responses to annual GH questionnaires on health are also included. Using a standardized abstraction form, trained abstractors reviewed the entire medical record for each subject, covering a median of 20 years of enrollment prior to AF diagnosis. Abstractors reviewed medical records for clinical care during the 6 months after AF onset and recorded each documentation of a warfarin prescription or a physician instruction to use aspirin, including date and daily dose prescribed.

Since 1977, the GH pharmacy database has included a record for each prescription dispensed or sold to GH enrollees from a GH pharmacy. Each record includes the drug,

strength, quantity dispensed, and intended days supply. Among patients in this age group, 96% of GH members report filling all or almost all prescriptions through GH pharmacies.⁶ Over-the-counter drugs, such as aspirin, can be purchased at GH pharmacies, and a record is created in the pharmacy database just as for prescription medications. Warfarin or aspirin use in the pharmacy records was defined as a dispensing or sale of the drug as recorded in the pharmacy database during the 6 months after AF onset.

We determined the sensitivity, specificity, and positive predictive value (PPV) as measures of the validity of the GH pharmacy database as compared with the medical record (gold standard) for warfarin use and for aspirin use during the first 6 months after AF onset. Because permanent AF is defined as AF that is present continuously for 12 months or longer,¹ the initial 6-month period after AF onset is a time when treatment decisions (including the decision about whether to use warfarin and aspirin) are being made and AF recurrence and persistence are being assessed. We also examined the narrower 3-month initial time period after AF onset to determine whether agreement would be substantially lower for a shorter time interval. We also report the κ statistic as a measure of the extent of agreement beyond chance alone.⁷ As another approach to potentially improve the sensitivity of the automated data for warfarin use, laboratory data on the international normalized ratio (INR) were considered along with the pharmacy data. Warfarin use was defined as having a dispensing for warfarin in the pharmacy database or an INR above the normal range (≥ 1.2) during the 6-month period after AF onset.

RESULTS

In the study population of 1953 newly detected AF cases, the mean age was 70.5 years (standard deviation 10.9), 47.8% were female and 92.1% were white. More than half of the subjects had hypertension (54.4%), 15.9% had diabetes mellitus, and 35.6% had a history of cardiovascular disease (stroke, angina, myocardial infarction, congestive heart failure, coronary revascularization, claudication, carotid endarterectomy, valvular heart disease, or peripheral vascular disease procedure). Few subjects (3.5%) were taking warfarin prior to their diagnosis of AF.

Among the newly detected AF cases, 1084 (55.5%) were identified in the medical record review as using any warfarin during the 6-month period after AF onset (Table 1). In comparison with the medical record review, the sensitivity, specificity, and PPV for the GH pharmacy database were excellent, and the κ statistic indicated almost perfect agreement. Results were similar for the 3-month period after AF onset.

According to the medical records, 51.5% (1005/1953) of subjects used aspirin at some point in the 6 months after AF onset (Table 1). Compared with medical record review, the GH pharmacy database had low sensitivity for aspirin use, but it had high specificity. The κ statistic represented only fair agreement for aspirin use. For the 3-month follow-up period, results were similar.

When laboratory data on INR were used in addition to the pharmacy data to define warfarin use, the sensitivity of these combined measures was slightly higher than the sensitivity of the pharmacy data alone (Table 1). However, specificity and PPV were lower.

DISCUSSION

We found that GH automated pharmacy data were in almost perfect agreement with medical record data for the use of warfarin in the 3 or 6 months following incident AF. With a high sensitivity, specificity, PPV, and κ , the GH pharmacy database appears to provide high-quality data on prescription warfarin for use in pharmacoepidemiologic research. However,

for aspirin use in the same period, the agreement between medical record review and the pharmacy data was only fair, indicating that aspirin use is not well captured by the GH pharmacy database for those with AF.

The study strengths include the completeness of both the medical record review data and the pharmacy data, the detailed information collected on medication use from the medical records, and the large proportion of GH members who fill their prescriptions at GH pharmacies.

There were also limitations to the study. While the study used population-based data, the findings may not be generalizable to non-GH automated pharmacy databases because of differences in the extent to which health plan members use the plan pharmacy. In addition, the study population may not be representative of members of other health plans since they had slightly higher socioeconomic status than the general population⁶ and were primarily of white race. A common limitation of pharmacy databases is that they contain data for dispensed prescriptions but not unfilled prescriptions or actual medication use. Additionally, we do not have information on the accuracy of physician notations of warfarin and aspirin use in the medical record. Thus, the medical record may not accurately reflect drug use, especially for over-the-counter drugs such as aspirin. Because aspirin is widely available without a prescription from non-pharmacy locations, aspirin purchases are not fully reflected in the GH pharmacy database.

Previous drug use validation studies have typically compared computerized pharmacy records to self-reported medication use^{8–10} or to medication container review.^{11,12} These studies encompassed a variety of study designs, populations, locations, and, in some cases, exposure periods. While aspirin or warfarin was not often assessed, in general, the measures of agreement found in our study were higher than previously reported. Lau *et al.*¹¹ evaluated ‘oral anticoagulants’ and ‘low-dose aspirin’. Compared to our results, sensitivity and PPV in Lau’s study were lower for the anticoagulants (75% sensitivity; 75% PPV) and higher for aspirin (93% sensitivity; 93% PPV) during the 3-month period before the date of medication container review among patients aged 70 years and older. This study was conducted in the Netherlands where low-dose aspirin is prescription only, and higher-dose aspirin can be obtained over-the-counter. There also may be differences between countries in data systems or drug availability from sources other than pharmacies.

Our findings suggest that the GH automated pharmacy database is a valuable source of data on warfarin use among patients with AF for pharmacoepidemiologic research. However, the database cannot be recommended for assessment of aspirin use. Replication of these findings in other health care plans is required before these conclusions can be widely generalized.

KEY POINTS

- Automated pharmacy databases are increasingly available for assessing medication use, but research on the validity of these data is incomplete.
- This study aimed to measure agreement on warfarin and aspirin use between medical records and automated pharmacy data among patients with newly detected atrial fibrillation (AF) at Group Health (GH), a large integrated health-care delivery system in Washington State.
- In comparison with the medical record review for warfarin use, the sensitivity, specificity, and positive predictive value for the GH pharmacy database were excellent, and the κ statistic indicated almost perfect agreement in the 3- and 6-month periods after AF onset.

- For aspirin use, the GH pharmacy database had low sensitivity but high specificity, and κ represented only fair agreement.
- The GH pharmacy database is a valuable source of data for pharmacoepidemiologic research on warfarin use among patients with AF. However, the database cannot be recommended for assessment of aspirin use.

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Agreement between automated pharmacy data (with or without laboratory data on INR) and medical record review data on the use of warfarin and of aspirin among patients with atrial fibrillation, Group Health, 2001–2004 ($n = 1953$)

Table 1

Warfarin use	Warfarin use by medical record review		Sensitivity		Specificity		PPV		κ
	Yes	No	%	95% CI	%	95% CI	%	95% CI	
Warfarin use in pharmacy data, interval after AF onset									
0–6 months									
Yes	1025	12							
No	59	857							
Total	1084	869	94.6	93.0–95.8	98.6	97.5–99.3	98.8	97.9–99.4	0.93 0.91–0.94
0–3 months									
Yes	987	11							
No	66	889							
Total	1053	900	93.7	92.1–95.1	98.8	97.8–99.4	98.9	98.0–99.4	0.92 0.90–0.94
Warfarin use in pharmacy data or elevated INR in laboratory data, interval after AF onset									
0–6 months									
Yes	1061	49							
No	23	820							
Total	1084	869	97.9	96.8–98.6	94.4	92.6–95.8	95.6	94.2–96.7	0.93 0.91–0.94
Aspirin use	Aspirin use by medical record review		Sensitivity		Specificity		PPV		κ
	Yes	No	%	95% CI	%	95% CI	%	95% CI	
Aspirin use in pharmacy data, interval after AF onset									
0–6 months									
Yes	376	52							
No	629	896							
Total	1005	948	37.4	34.4–40.5	94.5	92.8–95.8	87.9	84.3–90.7	0.31 0.27–0.36
0–3 months									

Warfarin use	Warfarin use by medical record review		Sensitivity		Specificity		PPV		κ
	Yes	No	%	95% CI	%	95% CI	%	95% CI	
Yes	302	33							
No	666	952							
Total	968	985	31.2	28.3–34.2	96.6	95.3–97.6	90.1	86.3–93.0	0.28
									0.24–0.32

PPV, positive predictive value; CI, confidence interval; INR, international normalized ratio.