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Complications of Warfarin Therapy: Causes, Costs, and the Role of the Anticoagulation Clinic

CONTEXT. Anticoagulation with warfarin requires careful management to avoid hemorrhage or thrombosis. The anticoagulation clinic has been suggested as a mechanism to reduce complications related to anticoagulation.

OBJECTIVE. To report our experience with anticoagulation complications, the cost of subsequent care, and the role of the anticoagulation clinic.

DESIGN. Sequential patients who were receiving warfarin within a period of 4 months were followed to identify warfarin-related adverse events. An independent examiner reviewed medical records to determine whether events were preventable and to identify possible causes. Hospital-based accounting data were used to determine attributable costs.

PATIENTS. 306 patients who received warfarin prescriptions at a rural Vermont university-affiliated VA hospital with an established anticoagulation clinic.

RESULTS. 91% (278) of patients received follow-up at the anticoagulation clinic, and the remaining 9% (28) were followed by VA physicians without involving the anticoagulation clinic. A total of 12 patients had adverse events associated with either sub- or supratherapeutic international normalized ratios, with an attributable cost of approximately \$90,000; 8 of these patients were not enrolled in the anticoagulation clinic. Thus, the estimated relative risk for adverse events for patients not at the clinic, compared with those who were, was almost 20 (95% CI, 6.4 to 61.8). Review of the remaining 4 patients revealed that their problems were attributable either to missed appointments or lack of coordination between other providers and the anticoagulation clinic.

CONCLUSIONS. Establishing an anticoagulation clinic is only the first step toward reducing complications related to anticoagulation. The larger challenge is ensuring that patients use the anticoagulation clinic and that providers communicate with it. Our results suggest that our institution could invest considerable resources to meet this challenge and still save money.

Warfarin is commonly used to anticoagulate patients for a variety of indications, both therapeutic (e.g., treating deep venous thrombosis, maintaining bypass graft patency) and prophylactic (e.g., preventing stroke in atrial fibrillation). However, warfarin has a narrow therapeutic window (i.e., it is easy to over or under dose) and is commonly associated with adverse events, mainly bleeding.¹ To reduce these events, use of special anticoagulation clinics for monitoring patients receiving warfarin has been advocated,²⁻⁵ and consensus guidelines for anticoagulation clinic organization and management have been published.⁶ Consequently, the number of health systems that use specialty anticoagulation clinics has increased.

This paper is available at ecp.acponline.org.

Although there has never been a randomized trial of anticoagulation clinics, the Anticoagulation Guidelines Task Force recently summarized several observational studies and reported a combined major hemorrhage rate of 11% per patient per year among patients receiving routine medical care versus 3% among patients in anticoagulation clinics.⁶ Many of these studies, however, were conducted when complication rates were higher than those of today (before standardized reporting of anticoagulation activity by using the international normalized ratio [INR]). In addition, the observational stud-

ies are all potentially confounded by selection bias. Specifically, independent factors of patients enrolled in anticoagulation clinics (e.g., above-average compliance and ability to engage the health care system) may contribute to observed improved outcome. These factors may also affect who participates in future randomized trials and may threaten their generalizability.

The challenge inherent in systems currently using an anticoagulation clinic model is in evaluating the experience of all patients receiving warfarin, including those who never enroll in clinic (or who miss their

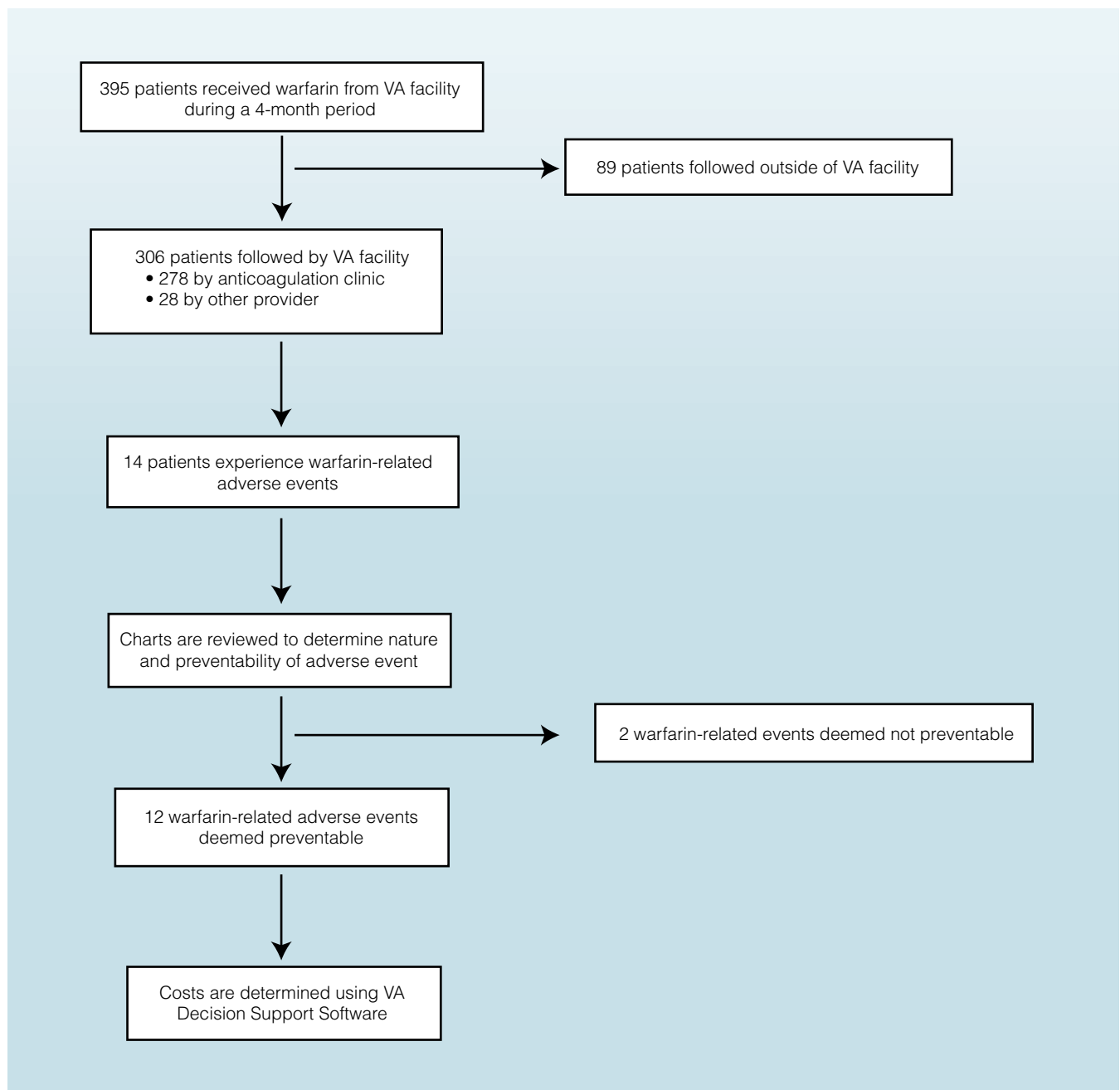


FIGURE 1. Overview of study design.

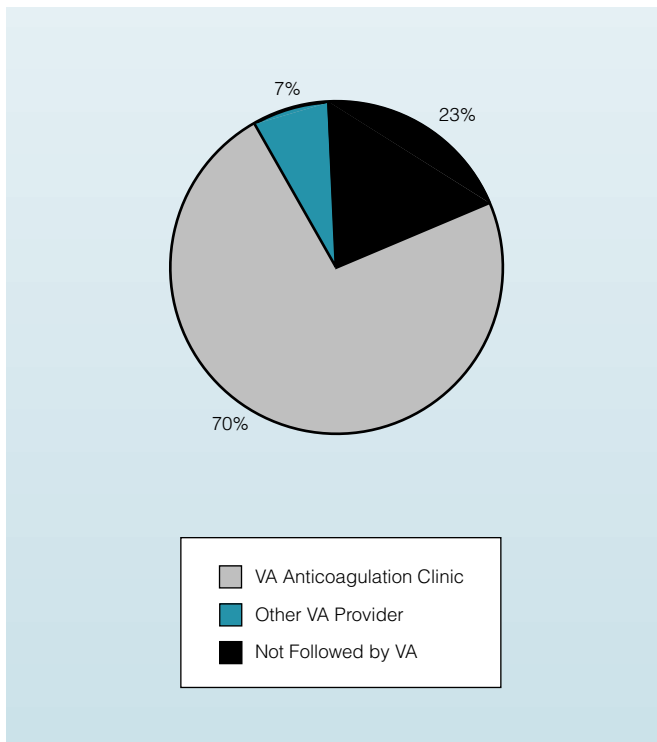


FIGURE 2. Source of follow-up for patients who were prescribed warfarin.

appointments) and who may or may not be managed by other providers.^{7, 8} It is equally important to determine the financial cost of failed care processes so that organizations can determine what resources might be devoted to improving the processes.⁹ In this case report, we sought to evaluate our system's experience with ambulatory patients receiving warfarin. Specifically, we ascertained the number, cause, and cost of preventable warfarin-related adverse events and identified opportunities for improvement.

Methods

Setting

The White River Junction VA facility is an acute care hospital in rural Vermont and part of the VA New England Network. Our facility currently has an established anticoagulation clinic staffed by a full-time Doctor of Pharmacology. Patients are referred to the clinic by their clinicians. In conjunction with the patient's referring physician or primary care provider, the pharmacist uses protocols to determine warfarin dosing and monitoring interval.

Patient Selection and Follow-up

Figure 1 provides an overview of our study design. During a 4-month period, one of us (LH), who had no

patient care responsibilities in the anticoagulation clinic, was electronically notified of each ambulatory patient receiving a warfarin prescription processed through the facility's pharmacy. Clinical information on all subsequent encounters for each patient in the cohort was collected by using the electronic medical record. Specifically, the investigator reviewed the location and frequency of follow-up monitoring and records of clinic visits or hospitalizations. Any encounter involving hemorrhage or thrombosis in patients who were prescribed warfarin were reviewed to determine whether the adverse event was preventable and to determine a possible cause. A *preventable warfarin-related adverse event* was defined as hemorrhage in a patient receiving warfarin who had an INR greater than 5 or thrombosis in a patient who had an INR less than 2. Clinical records of patient care encounters outside of the VA facility were not reviewed.

Cost

The cost of additional care given to patients experiencing warfarin-related adverse events was retrieved retrospectively from the VA Decision Support Software (DSS) cost accounting system. This system provides direct costs (variable and fixed) on the basis of a labor–time allocation strategy. Included in costs are labor; supplies; equipment depreciation; and a portion of professional services rendered, based on a calculated sum total of unit costs for all patient encounters related to adverse warfarin-related events. Cost estimates derived from DSS data are believed to be conservative.¹⁰

Results

During a 4-month period, 395 patients received prescriptions for warfarin and were monitored in a variety of settings (Figure 2). To learn more about why 89 patients were not followed by the VA, we performed a simple telephone survey and found that most thought the VA was too far from home (Figure 3).

We then focused on the 306 patients who were followed at the VA facility. Fourteen patients (5%) had a warfarin-related adverse event, including one death. Two of these events were judged not to be preventable—while receiving warfarin, one patient developed gastrointestinal hemorrhage from an ulcer and another had hemoptysis from a new pulmonary nodule. Both patients had therapeutic INRs.

Table 1 provides clinical details of the 12 events that were deemed preventable. Most events involved bleeding related to a supratherapeutic INR. Table 1 also shows that most patients who had adverse events were not enrolled in the anticoagulation clinic. In fact, the rel-

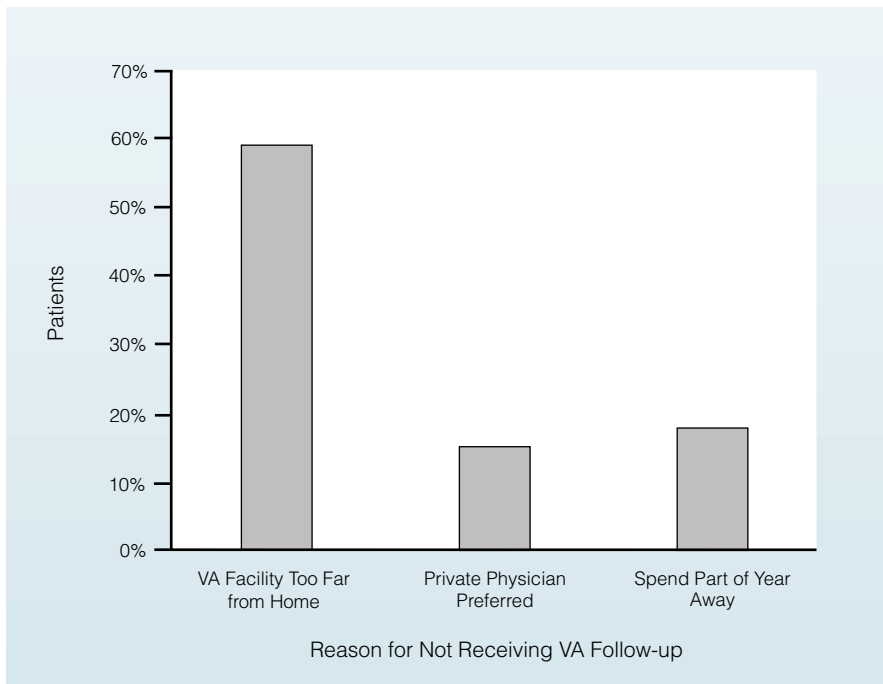


FIGURE 3. Reasons reported by patients for not receiving follow-up at the VA facility.

ative risk for adverse events among patients not enrolled in the anticoagulation clinic was 20 times that of enrolled patients ($[8 \text{ of } 28]/[4 \text{ of } 278] = 19.9$; CI, 6.4 to 61.8). For the four patients enrolled in the clinic, the adverse events were attributable to either missed appointments or lack of coordination between other providers and the anticoagulation clinic.

The cost of preventable warfarin-related adverse events during the 4-month study was \$90,000, suggesting an estimated annual cost of \$270,000. The cost of preventable warfarin-related adverse events in patients not followed by the anticoagulation clinic was 75% of the total cost of preventable warfarin-related adverse events identified.

Discussion

Our examination of the frequency and cause of warfarin-related adverse events in a single system showed that the events were common and generally involved patients who did not use the anticoagulation clinic. We also found the clinical sequelae and cost of these events to be significant. These results suggest that our institution, which uses an anticoagulation clinic, might invest considerable resources to improve the processes of care related to warfarin (as much as \$270,000 annually) and still save money. These results are consistent with those of others who have found potential savings in the use of anticoagulation clinics.^{11,12}

We believe that there are several ways our organization might respond to these findings. Most patients who

did not use the anticoagulation clinic reported that it was too far from home; we envision two possible solutions to this problem. The simplest would be to eliminate the practice of prescribing warfarin to patients who cannot be monitored by the VA facility. An alternate strategy would be to develop a monitoring system that does not involve traveling to the clinic, such as the telephone or self-monitoring. Another problem we found was failure to inform the anticoagulation clinic of important care events (e.g., surgery, liver biopsy, cardioversion, and hospital discharges). To address this, the anticoagulation clinic might be supplemented with case-management staff. Finally, to prevent missed anticoagulation clinic appointments, investing in patient tracking programs with clinical-decision support capabilities should be considered.¹³

Our study has several limitations. We have no information about the experience of patients who were not monitored at the VA facility. In addition, observation of patients monitored at the VA facility was limited in both time and scope. The length of observation (not more than 4 months) undoubtedly underestimated the warfarin-related adverse events of all study patients. The scope was limited to events within the VA facility and did not include the experience of patients who had an adverse event treated outside of the facility. These limitations make our results an underestimate of the total impact of warfarin-related adverse events.

Perhaps the greatest limitation is that our data in no way prove that moving all patients into an anticoagulation clinic (and providing better coordination) would have prevented their adverse events. Lack of perfect evi-

TABLE 1

Summary of Patients Having Preventable Warfarin-Related Adverse Events*

PATIENT	ENROLLED IN ANTICOAGULATION CLINIC?	ADVERSE EVENT	HOSPITALIZED?	CAUSE	OUTCOME	COST
Subtherapeutic INR (<2)						
1	No	Atrial fibrillation, splenic infarction	No	Missed follow-up	Full recovery	\$710
2	No	Thrombosis of leg bypass graft	Yes	Warfarin stopped for liver biopsy, failed to restart	Limb loss	\$10,927
3	Yes	Stroke	Yes	Missed follow-up with anticoagulation clinic	Recovered	\$11,917
4	Yes	Delay in cardioversion due to subtherapeutic INR	Yes	Cardioversion not coordinated with anticoagulation clinic	Planned cardioversion delayed	\$543
Supratherapeutic INR (>5)						
5	No	Hematoma	No	Not followed by anticoagulation clinic	Recovered	\$75
6	No	Wound hematoma	Yes	Warfarin dose at time of discharge not monitored	Recovered	\$825
7	No	Intra-abdominal bleeding	Yes	Discharged on warfarin, not monitored	Death	\$18,115
8	No	High INR noted during hospitalization for unstable angina	Yes	Patient not followed by VA and warfarin not recognized until heparin started	Delayed discharge from hospital by 2 days, recovered	\$245
9	No	GI bleed	Yes	Patient not monitored	Recovered	\$4,869
10	No	GI bleed	Yes	Patient not monitored	Transfused, recovered	\$33,487
11	Yes	GI bleed	Yes	Addition of Bactrim by nonanticoagulation clinic provider, which increased INR	Hospitalized 5 days, recovered	\$7,169
12	Yes	GI bleed	Yes	Missed follow-up with anticoagulation clinic	Recovered	\$2,453

*GI = gastrointestinal; INR = international normalized ratio.

dence, however, should not be used to support inaction. Organizational efforts should be made to avoid the adverse events described here. Getting all patients into the anticoagulation clinic would seem to be a logical place to start.

Establishing an anticoagulation clinic is only the first step toward reducing adverse events related to anticoagulation. The larger challenge is ensuring that patients use the anticoagulation clinic and that providers can easily communicate with it. These results suggest that our institution might invest considerable resources to meet this challenge and still save money.

Take-Home Points

- Because anticoagulation with warfarin requires careful management, many physicians have advocated specialized anticoagulation clinics.
- To learn about our facility's anticoagulation experiences, we reviewed the causes and costs of warfarin-related complications.
- Most adverse events occurred among the few patients who were not enrolled in the anticoagulation clinic.
- Reducing warfarin-related complications requires more than establishing an anticoagulation clinic: Patients and providers must be directed to use it.

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