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Full Length Article

The impact of new-onset cancer among veterans who are receiving warfarin for atrial fibrillation and venous thromboembolism☆

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ABSTRACT

Background: A new cancer diagnosis adds significant complexity and uncertainty to the management of pre-existing warfarin therapy.
Objectives: To determine how new-onset cancer affects anticoagulation control and outcomes among patients who had been receiving warfarin for atrial fibrillation (AF) compared to patients who had been receiving warfarin for venous thromboembolism (VTE) prior to cancer diagnosis.
Patients/methods: This cohort study started with 122,875 veterans who had been receiving warfarin for at least six months from a VA Medical Center between 10/1/06 and 9/30/08. We identified patients with incident cancer during this interval, and excluded those with a prior cancer history. We analyzed percent time in therapeutic range (TTR) at 6 and 12-month intervals after cancer diagnosis compared to pre-cancer baseline, as well as crude rates of warfarin-relevant outcomes (stroke, major bleeding, mortality) between patients with AF and VTE.
Results: Among patients with new-onset cancer, patients anticoagulated for AF outnumbered those anticoagulated for VTE more than 2.5-fold. There were no significant differences in TTR by indication for warfarin in months 0–6 or 7–12 following cancer diagnosis, but TTR decreased significantly compared to the pre-cancer baseline for both groups in months 0–6. As expected, cancer patients with VTE had significantly worse mortality at six months and one year compared to cancer patients with AF.
Conclusion: Patients receiving chronic warfarin therapy who are newly diagnosed with cancer experience a significant decrease in TTR in the first 6 months after diagnosis, regardless of indication for anticoagulation. This effect appears to attenuate in months 7–12.

1. Background

Warfarin therapy remains a mainstay of treatment for both atrial fibrillation (AF) and venous thromboembolism (VTE) for thousands of Americans as a means to reduce incidence of embolic stroke and recurrent VTE, respectively [1]. However, a new cancer diagnosis adds complexity and uncertainty to the management of anticoagulation for these patients. Previous work by our group has shown that patients who receive warfarin for any reason who are diagnosed with cancer will have worse anticoagulation control and worse outcomes (stroke, major hemorrhage, mortality) when compared to cancer-free controls [2,3].

However, it remains uncertain whether certain warfarin recipients are more vulnerable to these adverse effects of a new cancer diagnosis than others. Of particular concern is the group of patients who are chronically on warfarin for stroke prophylaxis in the setting of atrial fibrillation and are newly diagnosed with cancer. Although practice guidelines exist to guide clinicians in decision making for the management of cancer-associated VTE [4], no such guidance is available to clinicians who are caring for patients receiving warfarin for stroke prophylaxis in the setting of AF [5,6]. Compounding this gap in the literature is that AF is a much more common reason for chronic warfarin use than VTE [1], so there is a need to better understand the outcomes of AF patients following a cancer diagnosis and to develop an evidence based approach for managing such patients.

Because so little is known about this topic, any new information is valuable and can help draw attention to this understudied area. We therefore aimed to describe anticoagulation control and crude outcomes among patients newly diagnosed with cancer who had been receiving warfarin for AF, using patients with a new diagnosis of cancer who are receiving warfarin for VTE and also a group of cancer-free controls as reference. We hypothesized that anticoagulation control and outcomes related to warfarin therapy would be similar in the immediate post-cancer period between patients who receive warfarin for AF

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compared to those receiving it for VTE. We anticipate that this research will inform future studies seeking to establish rational population based strategies for warfarin continuation vs. alternative treatment strategies following a new cancer diagnosis.

2. Methods

2.1. Patient sample

All procedures were approved by the Bedford Veterans' Administration (VA) Institutional Review Board. This was a retrospective cohort study. We obtained encounter, demographic, laboratory and pharmacy fill data from the VA Clinical Data Warehouse and Medicare for 122,875 veterans who had ever received warfarin in a VA anticoagulation clinic from October 1, 2006 through September 30, 2008 (Fig. 1). Patients were deemed to have been receiving warfarin 1) while they were in possession of warfarin, defined as the duration of their most recent prescription fills plus a 30-day grace period and/or 2) during intervals between successive outpatient international normalized ratio (INR) tests of 42 days or less. For patients with a diagnosis of chronic liver disease, only the criterion based on possession of warfarin applied, as frequent INR testing could be to monitor chronic liver disease [7].

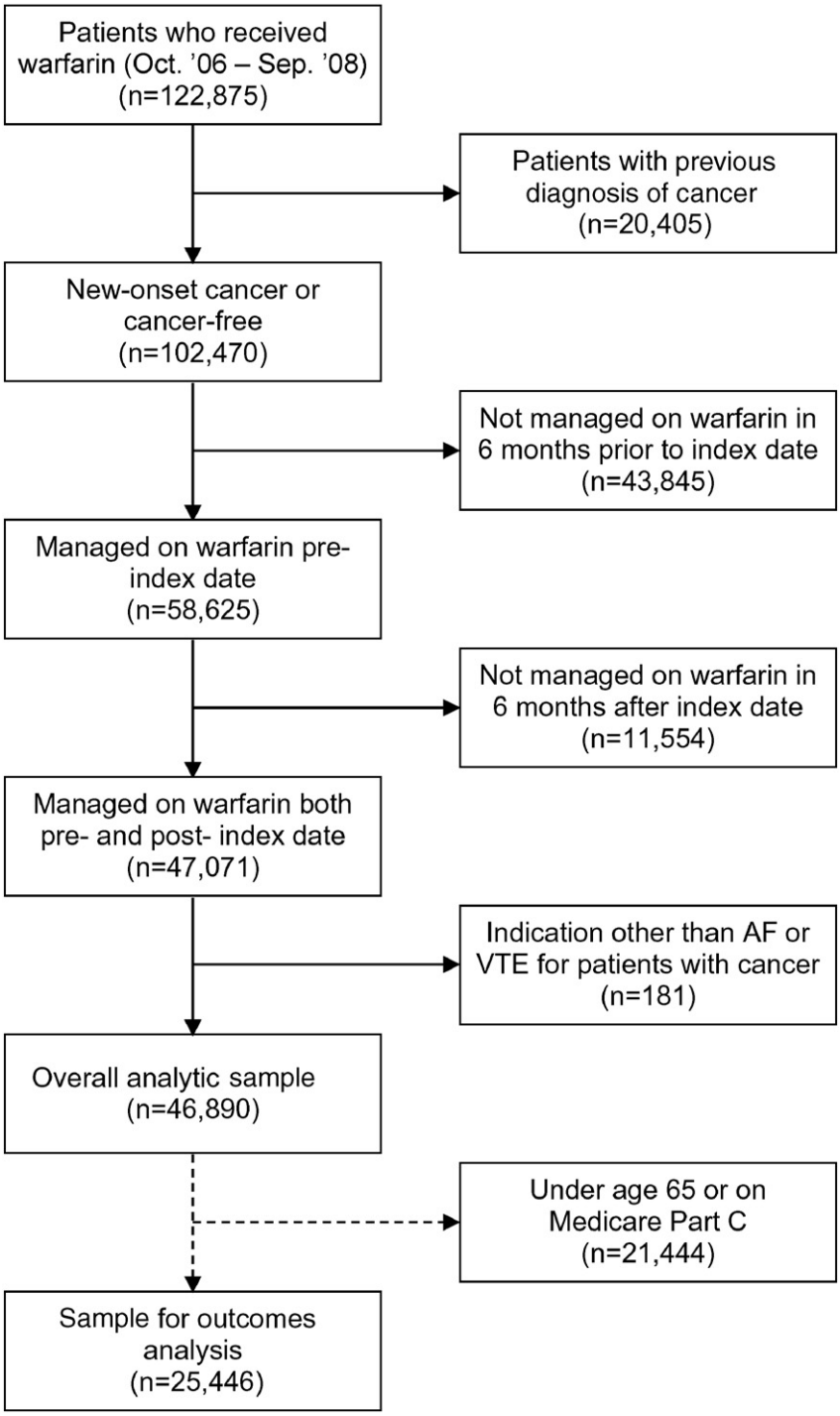

Fig. 1. Flowchart of patient sample constituents and exclusions.