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Prevalence and Clinical Intentions of Antithrombotic Therapy on Discharge to Hospice Care

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Abstract

Background: There are no guidelines for antithrombotic therapy on admission to hospice care. Antithrombotic therapy may offer some benefit in these patients, but is also associated with well-described risks.
Objective: We quantified the frequency and characteristics of patients prescribed antithrombotic therapy on discharge from acute care to hospice care.
Design: Retrospective cohort study.
Settings/Subjects: Adult (age>=21 years) patients discharged from acute care to hospice care between January 1, 2010 and June 30, 2014.
Measures: Our primary outcome of interest was receiving an outpatient prescription for antithrombotic therapy on discharge to hospice care.
Results: Among 1141 eligible patients, 77 (6.7%) patients received a prescription for antithrombotic therapy on discharge to hospice care, most frequently, aspirin (57.1%), enoxaparin (26.0%), and warfarin (20.8%). Patients actively treated for deep vein thromboembolism or pulmonary embolism, or with a history of atrial fibrillation or aortic/mitral valve replacement were significantly more likely to receive antithrombotic therapy. Patients with a history of cancer, cerebrovascular disease, or liver disease were significantly less likely to receive antithrombotic therapy ($p < 0.05$ for all). Among patients who received antithrombotic therapy, 22% were not receiving antithrombotic therapy before the index admission. Among patients previously receiving antithrombotic therapy, 55% continued on the same medication, of which 54.5% did not have any documented rationale for continuation.
Conclusions: Prescriptions for antithrombotic therapy were infrequent and often lacked a documented rationale. Further research is needed on the safety and effectiveness of antithrombotic therapy in hospice care and what drives current medication decisions in the absence of these data.

Keywords: anticoagulation; antithrombotic therapy; care transitions; hospice

Introduction

In the United States, hospice care is a team-based program for patients and their families, predominantly in their own homes, and funded by a per diem rate that must cover all services, medicines, supplies, and equipment related to the terminal illness during the last weeks to months of life.[1] Approximately, 40% of U.S. hospice patients are referred from an acute care hospital to hospice care.[1] This transition, which abruptly shifts goals of care from curative therapy to end-of-life palliative care, is an emotional and complex process for patients and their families.[2,3] In addition, patients, caregivers, and providers must sometimes make difficult decisions regarding patients' medication regimens. These decisions typically involve weighing patient preferences, perceived benefits, and risks of potential medical complications, while also ensuring that the patient's goals of care are met.

Antithrombotic therapy is frequently prescribed to patients with certain chronic diseases and in the acute setting for

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treatment and prophylaxis of thromboembolism and stroke.[4] Clinical guidelines support lifelong prophylaxis among patients with current thromboembolism or history of thromboembolism plus advanced cancer, although there is no guidance regarding discontinuation of therapy.[4] Hospice patients are at high risk of thromboembolism due to older age, prevalence of advanced cancer, and decreased mobility.[5] A previous study estimated that 10% of hospice patients have symptomatic thromboembolism and more than half of hospice patients have asymptomatic thromboembolism.[5] However, there is no clear palliative indication for antithrombotic therapy and the (United Kingdom) National Institute for Health and Care Excellence (NICE) guidelines note that thromboprophylaxis may not be appropriate for patients approaching end of life.[6] Antithrombotic therapy may be used for palliative management of deep vein thrombosis (DVT) to alleviate symptoms such as pleuritic chest pain, extremity swelling, or dyspnea.[6] However, these medications may only offer limited benefit in terms of stroke and thromboembolism prophylaxis in hospice due to frequent multimorbidity and limited life expectancy.[7] In addition, antithrombotic medications have well-known bleeding risks and are an important cause of adverse drug events requiring emergency department admissions.[8,9]

In this study, we quantified the frequency and clinical intentions of outpatient prescriptions for antithrombotic therapy on discharge from an academic tertiary care hospital to hospice care.

Methods

Study design

This was a retrospective cohort study of adult (age>=21 years) patients discharged directly from Oregon Health & Science University (OHSU) Hospital to hospice care between January 1, 2010 and June 30, 2014. Before study commencement, the OHSU Institutional Review Board approved this study.

During the study period, OHSU was a 544-bed, academic tertiary care facility in Portland, OR. Patients may have had multiple discharges to hospice care; however, we only included the first discharge to hospice care for each patient during the study period. We excluded patients if they died before hospital discharge or had an unknown discharge disposition. We also excluded patients who were admitted to the hospital for less than 24 hours or for observation purposes only (e.g., outpatient surgery).

Data collection

Patient identification and data collection methods have been described in a previous study on outpatient antibiotic prescriptions on discharge to hospice care.[10] Briefly, we obtained discharge disposition data for all patients discharged to hospice care from the OHSU Department of Care Management. We then obtained administrative, demographic, diagnosis, and medication data from the Pharmacy Research Repository (PHARR), a longitudinal repository of patient healthcare data developed in partnership with the OHSU Research Data Warehouse.

In addition, a pharmacist (C.A.K.) reviewed the medical records of all patients identified as having received a prescription for antithrombotic therapy on discharge. These reviews aimed to gain further insight into the prescriber's decision-making process by obtaining information from clinical notes, including the patient's history and physical, discharge summary, and palliative care consult notes. Medical record review was also utilized to validate medication orders and the indication for antithrombotic therapy, to determine if patients had been receiving antithrombotic therapy before hospital admission, and whether antithrombotic therapy prescribed on discharge was a continuation or de-escalation of therapy initiated on the index admission. All medical record data were entered into a secure database using Research Data Electronic Data Capture (REDCap).

Variable definitions

Our primary outcome of interest was receiving an outpatient prescription for antithrombotic therapy on discharge to hospice care. This was defined as medication orders for warfarin, enoxaparin, dalteparin, heparin, clopidogrel, dabigatran, rivaroxaban, apixaban, or aspirin (≤325 mg) in the patient's discharge summary. In addition, we determined whether antithrombotic therapy was de-escalated on discharge, which we defined as switching a patient from another agent to aspirin therapy, or if the dose was reduced from therapeutic to prophylactic. Our primary exposure of interest was the indication for anticoagulation therapy as was described in the discharge summary. Additional exposures of interest included demographic variables (e.g., age, sex), comorbid illnesses (identified using International Classification of Diseases, Ninth Revision [ICD-9] codes), length of hospitalization on the index admission, and patient preferences for life-sustaining treatment as documented on physician orders for life-sustaining treatment (POLST) form.[11] The POLST form is a set of medical orders that identify and communicate patients' wishes regarding medical treatment when they are seriously ill. In addition, we calculated CHADS2-VASc and HAS-BLED scores for all patients identified with atrial fibrillation.[12,13]

Statistical analysis

Descriptive statistics were calculated using means, standard deviations, and frequencies. Bivariable associations and multivariable logistic regression were used to examine the adjusted associations between patient and hospitalization characteristics and receiving an outpatient prescription for antithrombotic therapy upon discharge to hospice care. We used manual forward stepwise selection to determine the final model. Results from the multivariable model are presented as adjusted odds ratios (AOR) and 95% confidence intervals (CI). All analyses were performed using SAS statistical software, version 9.2 (SAS Institute, Cary, NC).

Results

This study included 1141 eligible patients who were discharged directly from OHSU Hospital to hospice care during the study period. The prevalence of receiving a prescription for antithrombotic therapy on discharge was 6.7% (77/1141) and the distribution of specific medications identified from each drug class is displayed in Table 1. Among patients discharged on antithrombotic therapy, the most frequently prescribed antithrombotic agents were aspirin at any dose (57.1%), followed by enoxaparin treatment or prophylaxis

(26.0%) and warfarin (20.8%). In addition, 18.2% of patients were discharged with prescriptions for more than one antithrombotic agent.

Characteristics of patients discharged directly to hospice care and bivariable analyses comparing patient characteristics by receipt of an outpatient prescription for antithrombotic therapy are displayed in Table 2. Approximately half of patients (51.4%) were aged 65 years or older, 54.5% were male, and 91.2% were Caucasian. In addition, 59.1% of patients had a diagnosis of cancer and 64.0% had a diagnosis of heart failure or cardiovascular disease. A POLST form was on file for 60.0% of patients discharged to hospice care and 81.7% of patients had a palliative care consultation during the index admission.

Patients discharged to hospice care with antithrombotic therapy were significantly more likely to have a hospital length of stay ≥7 days (50.7% vs. 39.0%; $p = 0.04$) compared to patients without a prescription. Age and hospice setting (inpatient vs. home) were not significantly associated with receiving antithrombotic therapy on discharge to hospice care. Patients with a comorbid diagnosis of renal disease were significantly more likely to receive a prescription for antithrombotic on discharge to hospice care (33.8% vs. 18.3%; $p < 0.01$), whereas patients with a history of cancer, liver disease, or cerebrovascular disease were significantly less likely to receive a prescription ($p < 0.05$ for all). Patients with an indication of atrial fibrillation ($p < 0.001$), heart valve replacement ($p < 0.001$), or active DVT treatment ($p = 0.04$) were more likely to receive a prescription for antithrombotic therapy. Among patients with atrial fibrillation, the mean (standard deviation) CHA2DS2-VASc score was 4.6 (1.7), while the mean (standard deviation) HAS-BLED score was 3.3 (1.3).

Table 3 displays unadjusted and adjusted associations with receiving a prescription for antithrombotic therapy on discharge to hospice care. Patients with comorbid diagnoses of cancer (AOR = 0.38, 95% CI = 0.22–0.64) or liver disease (AOR = 0.26, 95% CI = 0.09–0.73) were less likely to receive a prescription for antithrombotic therapy on discharge to hospice care. In addition, patients with cerebrovascular disease were less likely to receive a prescription for antithrombotic therapy (AOR = 0.26, 95% CI = 0.12–0.56). Alternatively, patients who were treated for a DVT or pulmonary embolism (PE) during the index admission (AOR = 2.7, 95% CI = 1.2–5.9), patients with a heart valve replacement (AOR = 4.3, 95% CI = 1.7–10.8), and patients with atrial fibrillation (AOR = 1.8, 95% CI = 1.1–3.0) were more likely to receive a prescription for antithrombotic therapy on discharge to hospice care.

Among patients discharged with a prescription for antithrombotic therapy, 77.9% (60/77) had received antithrombotic therapy before hospital admission and 22.1% (17/77) were initiated on antithrombotic therapy on discharge to hospice care. Among patients receiving antithrombotic therapy before the index hospitalization, 28.3% (17/60) had their therapy de-escalated on discharge to hospice care (data not shown). Table 4 displays the documented rationale that antithrombotic therapy was either continued or de-escalated. The most commonly documented rationale for de-escalation was increased bleeding risk relative to perceived benefit (58.8%), followed by perception of being more consistent with goals of care (29.4%), patient or family preference to discontinue the previous antithrombotic therapy (23.5%), and lack of indication for prior antithrombotic therapy (17.6%). Only 23 (53.5%) of the 43 patients, who continued antithrombotic therapy and were not de-escalated, had an explicitly documented rationale for this decision. Documented reasons for continuation included perceived indication for active treatment (34.9%) and patient or family preference to continue previous antithrombotic therapy (14.0%).

Table 1. Frequencies of Antithrombotic Agents Prescribed for Patients Discharged from the Hospital Directly to Hospice ($N = 77$)

	n (%)
Apixaban	2 (2.6)
Aspirin 81 mg	15 (19.5)
Aspirin 325 mg	20 (26.0)
Aspirin (no dose information)	9 (11.7)
Clopidogrel	6 (7.8)
Dabigatran	1 (1.3)
Enoxaparin treatment	15 (19.5)
Enoxaparin prophylaxis	5 (6.5)
Heparin	3 (3.9)
Warfarin	16 (20.8)

Fourteen (18.2%) patients were discharged with more than one antithrombotic agent.

Discussion

In this large cohort study of patients discharged directly from acute care to hospice care, ~7% of patients received an outpatient prescription for antithrombotic therapy. The most frequently prescribed antithrombotic agents were aspirin, enoxaparin, and warfarin. Several indications were independently associated with receiving an antithrombotic prescription including atrial fibrillation, active DVT or PE treatment on the index admission, and history of heart valve replacement, while patients with comorbid illness frequently favoring thromboprophylaxis (e.g., cancer) were significantly less likely to receive a prescription for antithrombotic therapy. Other notable findings were that 22% of the patients who received antithrombotic therapy on discharge to hospice care did not have documented receipt of antithrombotic therapy before the index admission. Furthermore, more than half (54.5%) of patients previously receiving antithrombotic therapy did not have charted rationale for continuation.

The prevalence of antithrombotic therapy on discharge from acute care to hospice has not been well described. A previous study reported that 18% of patients were receiving either therapeutic anticoagulation (12%) or thromboprophylaxis (6%) on admission to seven hospices in the United Kingdom.[5] However, it is unknown what proportion of these patients were admitted directly from acute settings compared to other referral sites. Other studies have reported that the prevalence of anticoagulation therapy in hospice ranges from 9% among hospice patients with lung cancer in the United States to 47% of patients across 21 palliative care units in Austria.[14,15] Our observed prevalence of 7% of patients is lower than these previous estimates. This may be due to inclusion of hospice patients with diagnoses not indicating antithrombotic therapy or be due to differences between the U.S. and European hospice systems.

Atrial fibrillation, heart valve replacement, and active DVT or PE treatment were significantly associated with

Table 2. Characteristics and Indications for Antithrombotic Therapy in Patients Discharged from the Hospital Directly to Hospice Care and Bivariable Analysis of Receiving an Outpatient Antithrombotic Therapy Prescription on Discharge ($N = 1141$)

Characteristic	*Total (*n = *1141)* n *(%)*	*Received antithrombotic therapy (*n = *77)* n *(%)*	*Did not receive antithrombotic therapy (*n = *1064)* n *(%)*	p
Age >65 years	586 (51.4)	43 (55.8)	543 (51.0)	0.41
Male sex	622 (54.5)	41 (53.3)	581 (54.6)	0.82
White race[a]	1018 (91.2)	72 (96.0)	946 (90.9)	0.44
Length of stay >7 days	454 (39.8)	39 (50.7)	415 (39.0)	0.04
Discharged to home hospice	672 (58.9)	48 (62.3)	624 (58.7)	0.53
POLST form completed before discharge	685 (60.0)	47 (61.0)	638 (60.0)	0.85
Palliative care consult during index admission	932 (81.7)	59 (76.6)	873 (82.1)	0.23
Comorbid diagnoses				
Cancer	674 (59.1)	31 (40.3)	643 (60.4)	<0.001
Chronic obstructive pulmonary disease	194 (17.0)	20 (21.1)	174 (16.6)	0.27
Cardiovascular disease	730 (64.0)	54 (70.1)	676 (63.5)	0.24
Cerebrovascular disease	235 (20.6)	9 (11.7)	226 (21.2)	0.045
Renal disease	221 (19.4)	26 (33.8)	195 (18.3)	<0.001
Liver disease	152 (13.3)	4 (5.2)	148 (13.9)	0.03
Indications				
Atrial fibrillation	261 (22.9)	32 (41.6)	229 (21.5)	<0.001
CHADS2-VASc; mean (SD)		4.6 (1.7)	—	—
HAS-BLED; mean (SD)		3.3 (1.3)	—	—
DVT/PE treatment on index admission	72 (6.3)	9 (11.7)	63 (5.9)	0.04
History of stroke	395 (34.6)	24 (31.2)	371 (34.9)	0.51
Heart valve replacement	26 (2.3)	8 (10.4)	18 (1.7)	<0.001
Total knee replacement/total hip replacement	45 (3.9)	4 (5.2)	41 (3.9)	0.54
Protein C and S deficiency/factor V Leiden mutation	8 (0.7)	2 (2.6)	6 (0.6)	0.1

[a]$n = 25$ patients were missing race ($n = 1116$, $n = 75$, $n = 1041$, respectively).
POLST, physician orders for life-sustaining treatment; SD, standard deviation; DVT/PE, deep vein thrombosis/pulmonary embolism.

Table 3. Adjusted and Unadjusted Associations between Patient Characteristics and Indications, and Receipt of an Outpatient Prescription for Antithrombotic Therapy Upon Discharge to Hospice Care ($N = 1141$)

Characteristic	*Unadjusted odds ratio (95% CI)*	*Adjusted odds ratio (95% CI)*
Age >65 years	1.2 (0.76–1.9)	
Male sex	0.95 (0.60–1.5)	
Race white	2.4 (0.74–7.8)	
Length of stay >7 days	1.6 (1.01–2.6)	
POLST form completed before discharge	1.0 (0.65–1.7)	
Palliative care consult during index admission	0.70 (0.41–1.2)	
Discharged to home hospice	1.2 (0.72–1.9)	
Comorbid diagnoses		
Cancer	0.44 (0.28–0.71)	0.38 (0.22–0.64)
Chronic obstructive pulmonary disease	1.8 (1.1–3.1)	
Cardiovascular disease	1.3 (0.81–2.2)	
Cerebrovascular disease	0.49 (0.24–1.0)	0.26 (0.12–0.56)
Liver disease	0.34 (0.12–0.94)	0.26 (0.09–0.73)
Renal disease	2.3 (1.4–3.7)	
Indications		
Atrial fibrillation	2.6 (1.6–4.2)	1.8 (1.1–3.0)
DVT/PE treatment on index admission	2.1 (1.0–4.4)	2.7 (1.2–5.9)
History of stroke	0.85 (0.52–1.4)	
Heart valve replacement	6.7 (2.8–16.0)	4.3 (1.7–10.8)
Total knee replacement/total hip replacement	1.4 (0.48–3.9)	
Protein C and S deficiency/factor V Leiden mutation	4.7 (0.93–24.0)	

CI, confidence interval.

Table 4. Rationale for Continuation or De-Escalation of Antithrombotic Therapy as Documented in Patient Medical Record ($N=60$)

	n (%)
Reason for continuation ($n=43$)	
Not addressed	20 (46.5)
Active treatment still indicated	15 (34.9)
Patient/family preference	6 (14.0)
Palliative	6 (14.0)
Prophylaxis still indicated	8 (18.6)
Benefit outweighs risk	1 (3.0)
Reason for De-escalation ($n=17$)	
Not addressed	2 (11.8)
Bleeding risk	10 (58.8)
Patient/family preference	4 (23.5)
No indication for prior anticoagulation	3 (17.6)
New contraindication	2 (11.8)
More consistent with palliative goals of care	5 (29.4)
Ease of monitoring	1 (5.9)

Percentages do not sum to 100% because prescribers may have documented more than reason for continuation or de-escalation.

receiving an outpatient prescription for antithrombotic therapy on discharge to hospice care. We hypothesize that clinicians may be more cautious when discontinuing antithrombotic therapy in these patients because of increased risk of stroke. However, we also observed that cancer, cerebrovascular disease, or history of stroke were not associated with receiving antithrombotic therapy. These results are evidence against that hypothesis and may reflect patient and provider expectations on whether antithrombotic therapy will improve the quality of remaining life. For example, if a patient is relatively stable and receives anticoagulation for atrial fibrillation, continuation of therapy may serve a palliative purpose because a new stroke could greatly decrease quality of life. In contrast, in a recent stroke patient, antithrombotic therapy may prolong life, but not affect overall quality of life. These conflicting results support the need for additional research on the safety and benefit of these medications to inform both patient and provider decision making and optimize therapy on transition to hospice care. For example, among patients with atrial fibrillation, the mean CHADS2-VASc score among patients with atrial fibrillation who received antithrombotic therapy was 4.6, which is consistent with current guidelines.[16] However, a pooled analysis of five randomized trials reported that the annual absolute risk reduction of stroke comparing warfarin to placebo in atrial fibrillation patients was 3.1%.[7] This relatively small risk reduction in light of potential risks of these medications and shortened life expectancy in hospice care suggest limited benefits of antithrombotic therapy in these patients. Neither this analysis nor the current guidelines specifically included or considered data from patients at end of life.

The observation that hospice patients received antithrombotic therapy for an active DVT or PE may serve a palliative purpose, as thrombosis can be associated with multiple distressing symptoms that may lower quality of life.[17] This observation is consistent with a previous study in which most patients received antithrombotic agents on hospice admission or active treatment rather than thromboprophylaxis.[5]

We defined de-escalation of antithrombotic therapy as switching from one antithrombotic agent to either prophylactic dosing or aspirin monotherapy. The most commonly documented reasons for de-escalation were perceived mitigation of bleeding risk or to align therapy with goals of palliative care. Although our data suggest this may be a relatively common strategy among providers, the potential benefits of de-escalation of antithrombotic therapy have not been evaluated in hospice patients or patients with limited life expectancy. Previous studies of elderly patients receiving antithrombotic therapy for atrial fibrillation suggest that the risk of major bleeding is not significantly lower among patients receiving aspirin compared to oral anticoagulants, but aspirin recipients were more likely to develop fatal or disabling stroke.[18] However, patients with a terminal illness were excluded from this study and the absolute annual risk reduction was only 2%. In the absence of definitive data, providers may feel more comfortable with therapy de-escalation in hospice patients due to decreased need for monitoring, convenience, or cost.

Our review of provider notes to better understand antithrombotic continuation or de-escalation suggests opportunities for improvement in documenting the rationale for these decisions. Nearly half of patients who were continued on antithrombotic therapy did not have a documented rationale for continuation. This is concerning given the lack of evidence to guide the use of antithrombotic agents in hospice. In addition, patient and/or family preferences were documented as rationales for both continuation and de-escalation; however, documentation of patient preferences on a POLST form was not associated with receiving a prescription or antithrombotic therapy on discharge. A review of 48 studies regarding patients' values and preferences for antithrombotic therapy identified considerable heterogeneity in these constructs.[19] Although these studies were not focused on patients at end of life, they support the need to understand and incorporate patient preferences in antithrombotic decision making. Better evidence leading to decision aids to support informed shared decision making is also needed.

The primary limitation of this study was that our retrospective study design likely did not capture the full antithrombotic medication discussion and decision-making process. Despite that we reviewed clinical notes in addition to patients' electronic health record data, this process is frequently not comprehensively documented in the electronic health record. In addition, our retrospective design also only allowed us to identify patients discharged directly to hospice care, and thus, patients who were initially discharged to nonhospice locations, but subsequently enrolled in hospice care shortly thereafter were not identified. Similar to our previous study of antibiotics on discharge to hospice, we hypothesize that these patients would be even more likely to receive an order for antithrombotic therapy on discharge because they had yet to enroll in a hospice and thereby forgo life-sustaining therapy.[10] In addition, because this study was focused on initiation or continuation of antithrombotic therapy, we did not identify and investigate patients who discontinued antithrombotic therapy on discharge to hospice care. Last, these data were collected between 2010 and 2014, and before the increased widespread use of direct-acting oral anticoagulants (e.g., apixaban or rivaroxaban). Thus, our results may underestimate the use of these agents in patients

discharging to hospice care. However, several factors, including cost and limited safety or efficacy data, preclude their use in hospice patients or patients with advanced disease or pronounced organ dysfunction.

Despite these limitations, this study provides the first data to our knowledge on the prevalence and documented clinical intentions of antithrombotic prescriptions on discharge to hospice care. Given the uncertainty regarding the benefits and harms of antithrombotic use in hospice care, these data are important as an initial step toward understanding which patients should receive antithrombotic therapy and why. Further research should build on these data to clarify the role of antithrombotic use in hospice care.

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Author Disclosure Statement

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