Appropriate Anticoagulation Management for Older Adults Living with Dementia

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Article

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Abstract: Anticoagulation and/or antiplatelet medication is recommended for individuals who have a history of atrial fibrillation, venous thromboembolism, acute coronary event or are post percutaneous coronary intervention. The purpose of this study was to describe the use of anticoagulants and antiplatelets among older adults living with dementia at hospital admission and 1 month follow up, treatments prescribed and associated complications. The sample included 404 hospitalized older adults living with dementia, the majority of whom were White females, mean age of 82 (SD=8). On admission 69% of the patients were on at least one anticoagulant or antiplatelet medication and at 1 month post discharge this decreased to 64%. At 1 month post discharge the percentage of individuals on two or more anticoagulants decreased from admission 34% to 14%. On admission 11 (4%) patients were admitted with adverse events from anticoagulation and at 1 month post discharge 5(2%) patients readmitted due to adverse events from anticoagulation. Given the risks and benefits of anticoagulation use among older adults living with dementia, a shared decision-making approach with patients and caregivers is recommended. This approach is the best way to help patients achieve their individual goals of care.

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There are a number of reasons anticoagulation is recommended including when there is a diagnosis of atrial fibrillation for the prevention of stroke [1], for patients post-acute coronary syndrome or post percutaneous coronary intervention [2], or for treatment and prevention of venous thromboembolism [3,4]. The benefits of anticoagulation are varied depending on the reason for treatment. Treating atrial fibrillation in all adults, for example, has been noted to reduce stroke risk by almost two-thirds [5]. For those with atrial fibrillation the CHA_2DS_2-VAS_c score is the most commonly used and validated tool to predict the risk of stroke and guide recommendations (Table 1) [1]. The risk of stroke is based on a score of ≥ 2 in men or ≥ 3 in women. In a recent study [6] with a sample of 8,294 patients with atrial fibrillation it was noted that all of the individuals 65 years of age and older, based on use of the CHA2DS2-VASc score, would have been started on anticoagulation. Thus there are concerns that the CHA2DS2-VASc score may have limited ability to discriminate those at high risk when used among older adults [7,8].

Table 1. Congestive Heart Failure, Hypertension, Age ≥75 (Doubled), Diabetes, Stroke (Doubled), Vascular Disease, Age 65 To 74 And Sex Category (Female) (CHA_2DS_2-VASc) Scores.

Variable	Criteria
Age	<65 (0); 65-74(1); ≥ 75(2)
Sex	Female (1); Male (0)
Congestive Heart Failure	No (0); Yes (1)

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Hypertension	No (0); Yes (1)
Stroke/TIA/Thromboembolism	No (0); Yes (1)
Vascular disease (myocardial infarction; peripheral artery disease; aortic plaque)	No (0); Yes (1)
Diabetes	No (0); Yes (1)

For individuals with atrial fibrillation who have had a recent percutaneous coronary intervention the recommendation is for triple therapy which is defined as one anticoagulant (e.g., apixaban, rivaroxaban, warfarin, dabigatran and enoxaparin) and two antiplatelet agents (e.g., aspirin and a $P2Y_{12}$ inhibitor such as clopidogrel, ticagrelor, prasugrel) for a short duration (depending on the risk of bleeding for the participant this is usually just for one month) [9]. This is then followed by combination therapy with an oral anticoagulant plus a $P2Y_{12}$ inhibitor for four to six weeks or up to 12 months, again depending on the risk level of the patient [10,11]. After 12 months in patients with atrial fibrillation and stable coronary artery disease not requiring any further intervention, the guidelines recommend monotherapy with an oral anticoagulant [10–12].

For patients with peripheral artery disease the consensus recommendation [13] is that asymptomatic patients should not be treated. Patients with ischemia should be given the option for platelet anti-aggregation with either low dose aspirin or a $P2Y_{12}$ inhibitor. A combination of aspirin with a low-dose of a direct oral anticoagulant (DOAC), specifically rivaroxaban, could be considered depending on the patients' risk factors for use of anticoagulation [14]. Patients at high risk of cardiogenic embolization should be considered for long term anticoagulation with a DOAC. These recommendations, however, are based on studies where the mean age of the participants was generally in the 70s (some with small numbers of individuals > 80 years of age), and the participants were competent and able to self-consent [14].

For individuals who have experienced a venous thromboembolism (VTE) there are guidelines for initiation of treatment and recommendations for use of long term treatment [3,4]. If there is a known cause (e.g., surgery) for the VTE, treatment can be stopped generally after three to six months. For those in whom the VTE was spontaneous, and no clear cause was identified, long-term treatment may be an option if the individual is not at high risk for bleeding. In a recent study comparing treatment of patients who had a VTE, it was noted that there was no difference in recurrence rates of VTE among those who did versus did not receive continued anticoagulation [15]. More bleeding occurred, however, among those who were on prolonged anticoagulation, with bleeding being most common for those on a standard dose DOAC compared to low dose DOACs.

Risk to Anticoagulation Use

There is a long list of risk factors that are associated with taking an anticoagulant as noted in Table 2 [16]. The major risk considered is bleeding, generally referred to as major bleeding or clinically relevant nonmajor bleeding (e.g., requiring a hospitalization or emergency room evaluation). Older adults particularly are at increased risk of subdural hematomas due to brain shrinkage and impact of the brain against the skull when there is any head trauma [17]. Bleeding risks are individually based and influenced by underlying disease and other medications [18,19]. There are also non-bleeding risk factors associated with anticoagulation use although these are less common and vary by type of treatment (Table 3).

Table 2. Factors Associated with Increased Risk of Bleeding with Use of Anticoagulants.

Factors Associated with Increased Risk of Bleeding
Age >65 years
A history of prior bleeding
A history of cancer, particularly metastatic disease
Renal impairment or failure
Liver impairment or failure
Thrombocytopenia

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Anemia
Poor anticoagulant control/medication adherence
Comorbidity and reduced functional capacity
Frequent falls
Alcohol abuse
Use of multiple anticoagulants

Table 3. Nonhemorrhagic Side Effects of Anticoagulants.

Aspirin	**Vitamin Antagonists Nonhemorrhagic Risk**	**KDOACs Nonhemorrhagic Risks**	**P2Y12inhibitor**
Allergic reactions including: hives; difficult breathing; swelling of the face, lips, tongue, or throat. Ringing in the ears Confusion Hallucinations Tachypnea Seizures Nausea/vomiting, Stomach pain Fever	Skin necrosis Limb gangrene Purple toe syndrome Possible vascular calcification, nephropathy, and orosteoporosis.	Dyspepsia Renal impairment Dizziness Headache Dyspnea Abdominal pain	Allergic response: skin rash, Itchiness, Flushing, or shortness of breath Thrombotic thrombocytopenic purpura (TTP) Diarrhea Muscle pain

The Benefits and Risks for Anticoagulation Among Older Adults Living with Dementia

Although there are clear benefits to use of anticoagulants in older adults for the prevention of stroke, myocardial infarction or an embolic event, these need to be considered against the significant risks. Further, the benefits may only be effective with certain treatment approaches (e.g., a decrease in myocardial infarction is only effective with rivaroxaban 2.5 mg and dual pathyway inhibition) [20]. The cost/benefit of the use of anticoagulation and/or antiplatelet treatment has not been well studied in older adults living with dementia. These individuals commonly experience transitions of care and changes in their primary health care providers and are unable to provide information as to why anticoagulation has been initiated. Through these transitions anticoagulants and/or antiplatelets may be continued or discontinued without a strong rationale to do so.

To get a sense of the current use of anticoagulants and/or antiplatelets used among older adults living with dementia during care transitions we evaluated use of these medications from admission to acute care to one month post discharge. Specifically, the percentage of individuals on anticoagulants and/or antiplatelets, the number of anticoagulants and/or antiplatelets prescribed, and evidence of associated bleeding with treatment on admission and at one month post discharge were evaluated. The findings from this study can be used to guide approaches for anticoagulation treatment among older adults living with dementia.

Methods

Design

This was a descriptive study using baseline data and one month follow up data from the study, Testing the Implementation of Function Focused Care in Hospitalized Older Adults Living with Dementia (R01AG065338; Clinicaltrials.gov NCT04235374). To participate, hospitals had to have a unit dedicated to medical patients. Patients were eligible to participate if they were 55 years of age or older, were admitted with a medical diagnosis, screened positive for dementia based on a score of ≤

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20 on the Saint Louis University Mental Status Examination [21], a score of > 2 on the AD8 Dementia Screening Interview[22], a score of 0.5 to 2.0 on the Clinical Dementia Rating Scale [23], and a score of ≥ 9 on the Functional Activities Questionnaire to differentiate between dementia and mild cognitive impairment [24]. Patients were excluded if they were enrolled in Hospice, on the unit for more than 48 hours, had no contact noted to provide follow up information, required surgery, or had a psychiatric or neurological problems that caused cognitive changes not due to dementia such as a brain tumor.

Procedures, Measures and Data Analysis

Data was collected by research evaluators based on chart review during the hospital stay (admission medications and diagnoses) and via telephone follow up at one month post discharge from the patient's caregiver/legally authorized representative. In addition, any adverse events including falls, emergency room transfers, hospital admissions and death were obtained during the telephone follow up. Demographic and descriptive information was also obtained from electronic health records and included reason for admission, age, gender, race, and comorbidities. Cognitive status was obtained using the Saint Louis Mental Status Exam (SLUMS) [21]. Descriptive analyses using SPSS 28.0 including means, standard deviations, frequencies and percentages were done to describe the sample, medication use and adverse events.

Results

The first 404 participants with medication data at admission and one month follow up were included in this analysis. The mean age of the participants was 82 (SD=8) and the majority were female (252, 62%) and White (282, 70%) older adults. The mean SLUMS was 7.7 (SD=6.0) and they had an average of 3 (SD=2) comorbidities. These individuals were from 10 hospitals. At the time of admission there were 124 (31%) individuals that were not on any anticoagulation or antiplatelet treatment with the remaining 280 (69%) on at least one anticoagulant or antiplatelet medication. As shown in Table 4, there were 187 patients (67%) out of the 280 treated on one anticoagulant or one antiplatelet medication, 83 individuals (30%) out of the 280 being treated that were on a combination of two medications with 67 on an antiplatelet and anticoagulant, 12 on two antiplatelet medications and 4 on two anticoagulants. There were 10 (4%) individuals out of the 280 being treated who were on three anticoagulants and antiplatelet medications. Of the 280 inidviduals on anticoagulants or antiplatelets on admission only 13 individuals (5%) had a clear reason documented in the medical record for treatment (atrial fibrillation, a venous thrombus embolism, or acute cardiac event based on admission diagnoses or comorbidities). Among the 280 participants on anticoagulation there were 11 individuals (4%) that were admitted due to a complication associated with anticoagulation (e.g., head trauma post fall, bleeding).

Table 4. Admission Anticoagulant or Antiplatelet Medications (280 Individuals on Treatment).

Admission Single Anticoagulant or Antiplatelet Medication	
Medication	Number of Individuals
Apixaban	42
Clopidogrel	7
Aspirin	69
Rivaroxaban	9
Dabigatran	2
Enoxaparin sodium injection	20
Heparin injection	30
Warfarin	8
Ticagrelor	0
	187 (67% of individuals on treatment)

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Admission Two Anticoagulant and/or Antiplatelet Medications	
Antiplatelet and Anticoagulant	
Clopidogrel and Heparin injection	6
Clopidogrel and Enoxaparin injection	2
Clopidogrel and Apixaban	4
Clopidogrel and Rivaroxaban	1
Aspirin and Heparin injection	24
Aspirin and Enoxaparin injection	17
Aspirin and Apixaban	7
Aspirin and Warfarin	3
Aspirin and Rivaroxaban	3
Antiplatelet and Antiplatelet	
Clopidogrel and Aspirin	10
Aspirin and Ticagrelor	2
Anticoagulant and Anticoagulant	
Rivaroxaban and Enoxaparin injection	1
Heparin injection and Enoxaparin injection	1
Heparin injection and Apixaban	1
Enoxaparin injection and warfarin	1
	83 (30%) of the 280 treated
Admission Three Anticoagulants and/or Antiplatelet Medications	
Clopidogrel, Heparin and Enoxaparin Injection	1
Aspirin, Apixaban, Enoxaparin injection	1
Aspirin, Enoxaparin and Heparin injection	1
Aspirin, Clopidogrel, Heparin injection	1
Heparin injection, Aspirin, Clopidogrel	2
Enoxaparin injection, Clopidogrel, Aspirin	1
Aspirin, Clopidogrel, Enoxaparin injection	2
Aspirin, Clopidogrel, Rivaroxaban	1

At one month post hospital discharge data was obtained on 340 (84%) out of the 404 participants. Among the missing 64 individuals, 25 (39%) died, 14 (22%) were unreachable and the others were pending follow up (25, 39%). As shown in Table 5, of the 340 individuals with follow up data there were 219 (64%) individuals on either an anticoagulant and/or an antiplatelet and 121 (36%) on no anticoagulation or antiplatelets. Of the 219, 188 (86%) were on one anticoagulant or antiplatelet treatment, 30(13%) were on a combination of an anticoagulant and antiplatelet treatment, and one individual (1%) was still on three drugs, two antiplatelet medications and one anticoagulant. At one month post discharge there were 5 individuals who had complications from anticoagulation and antiplatelet use. Two experienced internal bleeding and three experienced head traumas following falls.

Table 5. Month 1 Anticoagulant or Antiplatelet Medications.

Month 1 Single Anticoagulant or Antiplatelet Medication	
Medication	Number of Individuals
Apixaban	44
Clopidogrel	15
Aspirin	99
Rivaroxaban	13
Dabigatran	2
Enoxaparin sodium injection	1

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Heparin injection	2
Warfarin	10
Ticagrelor	0
Medication	Number of Individuals
Month 1 Double Anticoagulant and / or Antiplatelet Medication	
Antiplatelet and Anticoagulant	
Clopidogrel and Heparin injection	0
Clopidogrel and Enoxaparin injection	0
Clopidogrel and Apixaban	4
Clopidogrel and Rivaroxaban	1
Aspirin and Heparin injection	0
Aspirin and Enoxaparin injection	2
Aspirin and Apixaban	7
Aspirin and Warfarin	2
Aspirin and Rivaroxaban	2
Antiplatelet and Antiplatelet	
Clopidogrel and Aspirin	10
Aspirin and Ticagrelor	1
Anticoagulant and Anticoagulant	
Rivaroxaban and Enoxaparin injection	0
Heparin injection and Enoxaparin injection	0
Heparin injection and Apixaban	0
Enoxaparin injection and Warfarin	0
Month1 Three Anticoagulants and/or Antiplatelet Medications	
Medication	Number of Individuals
Aspirin, Enoxaparin injection, Warfarin	1

Over time there was a decrease in the percentage of older adults living with dementia that were on anticoagulation or antiplatelet therapy (Table 6). For those still being treated there was an increase in the number and percentage of inidivduals on a single anticoagulant or antiplatelet treatment and a decrease in the percentage of individuals on two and three treatments.

Table 6. Percentage of Older Adults Living with Dementia on Anticoagulants and Potentially Associated Complications Between Hospital Admission and One Month Post Discharge.

	Admission (N=404)		One Month Post Discharge (N=340)	
	On Anticoagulation N (%)	Not On Anticoagulation N (%)	On Anticoagulation N (%)	Not On Anticoagulation N (%)
Any Anticoagulant	280(69%)	124 (31%)	205(60%)	115(40%)
1 anticoagulant	186(66%)	-	176(86%)	-
2 anticoagulants	84(30%)	-	28(13%)	-
3 anticoagulants	10(4%)	-	1(1%)	-
Adverse events Associated with Anticoagulants	11(4%)	-	5(2%)	-

Discussion

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The rates of anticoagulation and antiplatelet use in our current study of older hospitalized patients living with dementia were similar to prior research evaluating all adults across different sites of care (e.g., home, nursing home, hospital) with rates ranging from 48% to 83% [25,26]. In our sample there was a slight decrease in anticoagulation and antiplatelet use over one month post discharge but this was still at 60%. There was also a decrease noted in the percentage of individuals on multiple drugs.

The impact of anticoagulation and antiplatelet use in this study noted that 4% of the study participants were admitted to the hospital with major bleeding associated events and 2% had major bleeding associated events at one month post discharge. This was consistent with an older 2006 study that reported the major risk of bleeding for individuals on anticoagulants or antiplatelets ranged from 1 to 3% [27]. In a recent 2023 study, however, the rate of bleeding was higher at 10% [28]. Our low rates may be due to incorrect admission or readmission diagnoses as the noted admission diagnosis may not have been accurate.

Making Treatment Decisions

The rates of known adverse events associated with anticoagulant or antiplatelet use was low in this study. Further, we do not know if anticoagulation treatment prevented a cardiovascular event. Given the known benefits [29,30] as well as the known risks associated with use of these medications [16,17,31,32] it is challenging to know what treatment recommendations to make when working with older adults living with dementia. Benefits may be particularly limited for nursing home residents living with dementia as prior research noted that treatment with oral anticoagulants or antiplatelets for atrial fibrillation provided only a modest benefit for risk of death with a promise of 76 days of longer life and no protection against stroke [31]. Risks of bleeding increase with the use of dual or triple antithrombotic therapy [30]. It is therefore critically important to establish if and when use of anticoagulants and/or antiplatelets are needed. This requires getting information from prior providers to determine the rationale for use (e.g., dates of cardiovascular procedures or events, history of atrial fibrillation).

Taking a Person-Centered Care and a Shared Decision-Making Approach

Guidance for anticoagulation use among older adults, particularly those living with dementia and those greater than 90 years of age is vague and recommends the use of "careful consideration" when making treatment decisions [30]. In situations in which there are not clear data to guide practice such as what we have seen with regard to some immunizations [33], a shared decision making and a person-centered approach may be the most appropriate way to proceed. Person-centered care is focused on engaging the individual or their legally authorized representative in shared decision making around a care related topic. Helping older adults living with dementia and their legally authorized representatives understand the benefits and risks associated with anticoagulation and antiplatelet use and identifying their goals of care, can help these individuals establish what risk they are willing to take. Documentation of this discussion and ongoing evaluation of the use of anticoagulation and antiplatelet use should also be done. With increased opportunities for treatment in terms of number and types of drugs available, our understanding of the risk and benefits associated with anticoagulation will develop as new data is accrued. For now, the person-centered shared decision-making approach may be the safest and most appropriate way to address anticoagulation among older adults living with dementia.

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