ORIGINAL RESEARCH

Evaluation of the Appropriateness of Aspirin Therapy in a Veteran Population

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Background: Aspirin is commonly used for primary and secondary prevention of atherosclerotic cardiovascular disease (ASCVD) but may cause more harm than benefit. This study aimed to assess the percentage of patients who were inappropriately prescribed aspirin in the veteran patient population and to assess safety outcomes associated with inappropriate aspirin use.

Methods: Retrospective chart reviews were conducted on up to 200 patients with active prescriptions for 81-mg aspirin tablets filled between October 1, 2019, and September 30, 2021, at the Captain James A. Lovell Federal Health Care Center in Illinois. The primary endpoint was the percentage of patients inappropriately on aspirin therapy and whether these patients were being followed by a clinical pharmacy practitioner. Each patient record was reviewed to determine the appropriateness of aspirin therapy by assessing the indication for use. Safety data were collected for patients who were deemed to be using aspirin inappropriately, including documentation of any major or minor bleeding events.

Results: A total of 105 patients were included in this study. For the primary endpoint, 31 patients (30%) had a possible ASCVD risk and were taking aspirin for primary prevention, while 21 patients (20%) had no ASCVD and were taking aspirin for primary prevention. For the secondary endpoint, 25 patients were aged > 70 years, 15 patients were concurrently taking medications that might increase bleeding risk, and 11 patients had chronic kidney disease. Looking at the entire study patient population, for the safety endpoint, 6 patients (6%) experienced a major bleeding event while on aspirin, and 46 (44%) experienced a minor bleeding event while on aspirin.

Conclusions: Common factors seen in this study to warrant deprescribing aspirin for primary prevention included individuals aged > 70 years, concurrent use of medications that increase bleeding risk, and patients with chronic kidney disease. By assessing ASCVD and bleeding risks and having a risk/benefit discussion with patients and prescribers, aspirin used for primary prevention can be appropriately deprescribed when the risks of bleeding outweigh the benefits.

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Aspirin is an antiplatelet agent that binds irreversibly to COX-1 and COX-2 enzymes, which results in decreased prostaglandin and thromboxane A2 production and inhibition of platelet aggregation. Aspirin often is used for its antipyretic, analgesic, and antiplatelet properties. Its use in cardiovascular disease (CVD) has been studied extensively over the past few decades, and recent data are changing the framework for aspirin use in primary prevention of atherosclerotic cardiovascular disease (ASCVD). Primary prevention refers to efforts to prevent the incidence of cardiovascular events, whereas secondary prevention refers to efforts to prevent a cardiovascular event after one has occurred.[1] This differentiation is important as it guides the course of treatment.

Three trials published in 2018 evaluated aspirin use in primary prevention of ASCVD. The ASCEND trial evaluated aspirin use for primary prevention of ASCVD in patients with diabetes mellitus (DM). This study concluded that although aspirin prevented serious vascular events in patients with DM, the benefit observed was largely counteracted by the bleeding hazard.[2] The ARRIVE trial evaluated aspirin use for primary prevention in patients with a moderate CVD risk. The study concluded that aspirin use in patients at moderate risk of CVD could not be assessed due to the low incidence rate of CVD; however, the study concluded that aspirin did not reduce the incidence of cardiovascular events for patients at low CVD risk and that aspirin caused more mild gastrointestinal bleeds compared with placebo.[3] The ASPREE trial evaluated aspirin use for primary prevention in patients aged > 70 years to determine whether its use prolonged a healthy lifespan. This trial concluded that patients who received daily aspirin were at a higher risk of major hemorrhage and that aspirin did not diminish CVD risk compared with placebo.[4]

These studies led to a paradigm shift in therapy to reevaluate aspirin use for primary prevention. Current indications for aspirin include secondary prevention of ASCVD (ie, myocardial infarction [MI], coronary artery bypass graft, transient ischemic attack [TIA], and stroke), venous thromboembolism prophylaxis in the setting of orthopedic surgery, or valvular disease with replacement and analgesia.

It is important to note that certain clinical circumstances may warrant aspirin use for primary prevention of ASCVD on a patient-specific basis, and this decision should be made using a risk/benefit analysis with the patient.

In April 2022, the US Preventive Services Task Force (USPSTF) recommended against using low-dose aspirin for primary prevention of ASCVD in individuals aged ≥ 60 years. The USPSTF noted that for patients who have a ≥ 10%, 10-year CVD risk, the decision to initiate aspirin should be based on a risk/benefit discussion and may be beneficial in certain patient populations.[5]

A 2019 National Heart, Lung, and Blood Institute survey found that 29 million Americans used aspirin for primary prevention of ASCVD, and 6.6 million of these Americans used aspirin for primary prevention without the recommendation of a health care professional (HCP). Almost half of these individuals were aged > 70 years and, therefore, at an increased risk for bleeding.[6] With the recent studies and changes in guidelines highlighting a higher risk rather than benefit with the use of aspirin for primary prevention, the current use of aspirin for primary prevention in the United States needs to be readdressed.

HCPs should assess the appropriateness of aspirin use in their patients to ensure that the risks of aspirin do not outweigh the benefits. Pharmacists can play a vital role in the assessment of aspirin for primary prevention during patient visits and make recommendations to primary care practitioners to deprescribe aspirin when appropriate.

METHODS

The objective of this study was to evaluate the appropriateness of aspirin therapy in patient aligned care team (PACT) clinics at the Captain James A. Lovell Federal Health Care Center (FHCC) in North Chicago, Illinois. The PACT clinics are a category of clinics that include all the primary care clinics at FHCC.

The primary outcome of this study was to determine the percentage of patients inappropriately on aspirin therapy. To assess the inappropriate use of aspirin, relevant history of ASCVD was collected. Patients were divided into 3 groups: those with a history of ASCVD, those with no risk factors or history of ASCVD, and those with risk factors and no history of ASCVD. Patients were then categorized for their indication for aspirin use, which included either primary or secondary prevention of ASCVD. Patients were categorized into the primary prevention group if they had no history of ASCVD, whereas patients with a history of ASCVD were placed into the secondary prevention group.

ASCVD was defined as patients with acute coronary syndrome (ACS), history of MI, stable or unstable angina, coronary or other arterial revascularization, stroke, TIA, or peripheral artery disease (PAD), including aortic aneurysm (all with an atherosclerotic origin). Possible ASCVD risk was defined as patients with DM with a major risk factor (family history of premature ASCVD, hypertension, dyslipidemia, smoking, chronic kidney disease [CKD]/albuminuria) or patients diagnosed with coronary artery disease without an event. The percentage of patients followed by a PACT pharmacist, the number of pharmacist follow-up visits during the study period, and the date of the first 81-mg aspirin pharmacy order that was filled at FHCC were also collected.

The secondary outcome of this study focused on patients who were using aspirin for primary prevention and assessed potential reasons that may warrant deprescribing aspirin therapy. One reason for deprescribing is that aspirin may not be indicated for some patients, including those with DM without cardiovascular complications, patients aged > 70 years, and/or patients with CKD (defined as estimated glomerular filtration rate < 60 mL/min). Another reason for deprescribing is contraindication, which included patients with coagulopathy, thrombocytopenia (defined as platelet count < 150,000 mL), a history of gastrointestinal bleeding, peptic ulcer disease or other major bleeds, and/or consistent use of medications that increase bleeding risk (such as nonsteroidal anti-inflammatory agents, steroids, or anticoagulants) for > 14 days.

The safety outcome of this study assessed bleeding events while on aspirin

TABLE Baseline Characteristics

	Total (N = 105)	Primary prevention (n = 52)	Secondary prevention (n = 53)
Mean age, y	72	69	75
Race, No. (%)			
African American	22 (21)	15 (29)	7 (13)
Other	3 (3)	1 (2)	2 (4)
Unknown	9 (9)	5 (10)	4 (8)
White	71 (68)	31 (60)	40 (75)
Pharmacy intervention			
PharmD follow-up, No. (%)	34 (32)	15 (29)	19 (36)
Mean No. of follow-up appointments	7	4	9
Date of aspirin initiation, No. (%)			
Before 2019	71 (68)	38 (73)	33 (62)
After 2019	34 (32)	14 (27)	20 (38)

therapy. All patients were categorized depending on if they had a major, minor, or no bleeding event while on aspirin therapy. Hemorrhagic stroke, symptomatic intracranial bleeding, bleeds located in other critical sites or organs (intracranial, intraspinal, intraocular, retroperitoneal, intraarticular or pericardial), bleeds causing hemodynamic instability requiring vasopressors, bleeds causing a > 2 g/dL hemoglobin drop since initiation of aspirin therapy, severe extracranial bleeding requiring transfusion or hospitalization, fatal bleeding, or bleeds requiring > 2 units of red blood cell transfusion were considered major bleeding events. Minor bleeding events were any events that did not meet the criteria for major bleeding, including bruising, bleeding gums, epistaxis, hemorrhoidal bleeds, and bleeding that did not require intervention or treatment.[7]

Patients were included if they were aged > 18 years, had an active prescription for 81-mg aspirin tablet on September 30, 2021, and were seen in FHCC PACT clinics or at affiliated community-based outpatient centers. Other doses of aspirin were excluded as the 81-mg dose is the standard dose for primary prevention of ASCVD in the United States. US Department of Defense patients, home-based primary care patients, and community living center patients were excluded in this study. Patients with an aspirin prescription from a non–US Department of Veterans Affairs (VA) facility and patients on aspirin for reasons other than cardiovascular protection (such as pain, fever, etc) also were excluded from this study.

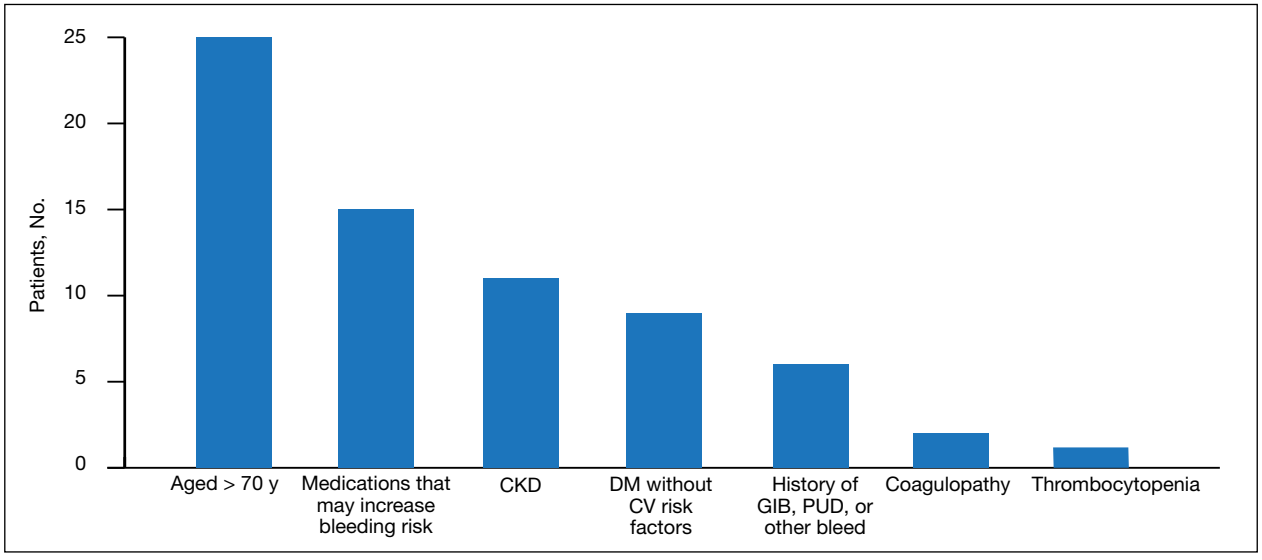
Data were collected from the FHCC electronic health record. A list was generated to include all active prescriptions for aspirin filled at FHCC as of September 30, 2021. Data were reviewed before this date to capture primary and secondary outcomes. No information was gathered from the chart after that date. This project was approved by the Edward Hines, Jr. VA Hospital Institutional Review Board. The primary and secondary outcomes were reported using descriptive statistics.

RESULTS

This study reviewed 140 patient records and 105 patients met inclusion criteria. The mean age of patients was 72 years overall, 69 years in the primary prevention group, and 75 years in the secondary prevention group. Of the 105 patients reviewed, 32% of patients (n = 34) were followed by a pharmacist (Table).

For the primary endpoint, 53 patients (50%) were on aspirin for secondary prevention and 52 (50%) were on aspirin for primary prevention. Of the 105 patients included in the study, 31 (30%) had a possible ASCVD risk and were taking aspirin for primary prevention, while 21 (20%) had no ASCVD and were taking aspirin for primary prevention. Of the 52 patients on aspirin for primary prevention, 31 patients (60%) had a possible risk for ASCVD. Of the 52 patients in the primary prevention group, 15 (29%) were followed by a

FIGURE Factors That May Warrant Deprescribing Aspirin Therapy for Primary Prevention (N = 52)



Abbreviations: CKD, chronic kidney disease; CV, cardiovascular; DM, diabetes mellitus; GIB, gastrointestinal bleed; PUD, peptic ulcer disease.

pharmacist, and the average number of follow-up appointments was 4.

The secondary endpoint focused on patients taking aspirin for primary prevention and the factors that may warrant deprescribing aspirin. Of the 52 patients on aspirin for primary prevention, 25 patients were aged > 70 years, 15 patients were concurrently taking medications that may increase bleeding risk, 11 patients had CKD, 9 patients had DM and no CVD risk factors, 6 patients had a history of gastrointestinal bleeding, peptic ulcer disease, or other bleeding event, 2 patients had coagulopathy, and 1 patient had thrombocytopenia (Figure).

For the entire study group, 6 patients (6%) experienced a major bleeding event while on aspirin, 46 (44%) experienced a minor bleeding event while on aspirin, and 53 (50%) experienced no bleeding events while on aspirin. Of the 6 patients who experienced major bleeding events, 4 were on aspirin for secondary prevention, and 2 were on aspirin for primary prevention with ASCVD risk factors. The major bleeding events included 4 gastrointestinal bleeds, 1 intracranial hemorrhage, and 1 hemorrhagic stroke. Of the 46 who experienced minor bleeding events, 20 patients were on aspirin for primary prevention; 11 of those patients had possible ASCVD risk factors and 9 had no documented ASCVD. The minor bleeding events included hematuria, epistaxis, bleeding scabs, and dental bleeding.

DISCUSSION

The majority of patients in this study were on aspirin appropriately. Indications deemed appropriate for aspirin therapy include secondary prevention and primary prevention with a possible ASCVD risk. About 20% of the total patient population in this study was taking aspirin for primary prevention with no ASCVD risk. For these patients, the risk of bleeding likely outweighs the benefits of aspirin therapy as patients are at low risk for ASCVD; therefore, aspirin therapy is likely inappropriate in this patient population. These patients may be unnecessarily at an increased risk for bleeding and may benefit from deprescribing aspirin. For the safety of patients, HCPs should be continuously assessing the appropriateness of aspirin for primary prevention and deprescribing when necessary.

About one-third of the patients using aspirin for primary prevention were followed by a pharmacist. Pharmacists can play a key role in deprescribing aspirin for primary prevention when aspirin use is deemed inappropriate. About 30% of the total patient population in this study was on aspirin for primary prevention with

possible ASCVD risk. This patient population may benefit from aspirin therapy as they are at a higher risk for ASCVD. For these patients, a risk/benefit discussion is necessary to determine the appropriateness of aspirin for primary prevention. This risk/benefit discussion should be a continuous conversation between patients and HCPs as different factors such as age and changes in comorbid conditions and medications may increase bleeding risk.

The secondary endpoint focused on patients taking aspirin for primary prevention and the factors that may warrant deprescribing aspirin. The most common factors seen in this study included patients who were aged > 70 years, patients who were concurrently taking medications that may increase bleeding risk, and patients with CKD. All of these factors increase bleeding risk, making the risks potentially outweigh the benefits of aspirin for primary prevention. These factors should be the primary focus when assessing patients on aspirin for primary prevention to promote deprescribing aspirin if deemed appropriate as they were the most prevalent in this study.

The safety endpoints focused on bleeding events as a whole as well as the bleeding events seen in the primary prevention group. There were 2 major bleeding events and 20 minor bleeding events in the primary prevention group. The number of bleeding events both major and minor further shows the need for a continuous risk/benefit discussion between patients and HCPs on continued aspirin use for primary prevention. The bleeding risk with aspirin is prevalent. HCPs should continue to assess for factors that increase the bleeding risk that may warrant deprescribing aspirin to prevent future bleeding events in this patient population.

Strengths and Limitations

As there have been recent updates to guidelines on the use of aspirin for primary prevention, a strength of this study is that it evaluates a topic that is relevant in health care. Another strength of this study is that it focuses on specific patient factors that HCPs can assess when determining whether aspirin for primary prevention is appropriate in their patients. These specific patient factors can also be used as a guide to help HCPs deprescribe aspirin for primary prevention when appropriate.

One of the limitations of this study is that bleeding events that occurred outside of the FHCC were unable to be assessed unless the HCP specifically commented on the bleeding event in the chart. This could potentially underestimate the bleeding events seen in this study. Another limitation is that the bleeding risk for patients who were not on aspirin was not assessed. There was no comparison group to ascertain whether the bleeding risk was higher in the aspirin group compared with a no aspirin group. However, many of the major clinical trials saw an increased risk of bleeding in the aspirin group compared with placebo.

CONCLUSIONS

Aspirin therapy for secondary prevention remains an important part of treatment. Aspirin therapy for primary prevention may be appropriate for patients with a possible ASCVD risk. The therapy may be inappropriate in cases where patients have an increased bleeding risk and low or no ASCVD risk. It is important to continuously assess the need for aspirin therapy for patients in the setting of primary prevention. Common factors seen in this study to warrant deprescribing aspirin for primary prevention include patients aged > 70 years, concurrent use of medications that increase bleeding risk, and patients with CKD. By assessing ASCVD risk as well as bleeding risk and having a risk/benefit discussion between the HCP and patient, aspirin used for primary prevention can be appropriately deprescribed when the risks of bleeding outweigh the benefits.

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Ethics and consent

Since this study is retrospective in nature, it presents no more than minimal risk of harm to patients and involves no procedures that would require written consent. This project was approved by the Edward Hines, Jr. Veterans Affairs Hospital Institutional Review Board.

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