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Research paper

Impact of pharmacist intervention to deprescribe inappropriate aspirin therapy in an outpatient anticoagulation clinic at a community hospital☆

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ABSTRACT

Study objective: This study describes a pharmacist-led process to identify and discontinue inappropriate aspirin in patients receiving concomitant anticoagulant therapy and to evaluate the effectiveness of the intervention.
Setting: The study took place in an outpatient anticoagulation clinic within a small community hospital.
Participants: Patients ≥40 years old on indefinite anticoagulation therapy for atrial fibrillation and/or venous thromboembolism were included.
Design: This is a quality improvement initiative.
Interventions: Utilizing the electronic medical record and patient interview, use and indication for daily aspirin therapy was confirmed. Prospectively collected patient demographics and past medical history were used to determine appropriateness of aspirin therapy. For patients identified as receiving inappropriate aspirin therapy, a fax was sent to the referring provider recommending aspirin discontinuation.
Main outcome measures: To assess the effectiveness of the intervention, outcomes were retrospectively measured. The primary outcome was the percentage of "accepted" recommendations. Secondary outcomes included the prevalence, dosing, and indications for aspirin therapy.
Results: Eighty (33 %) of 242 patients were on aspirin. Fifty-two patients with atrial fibrillation and/or venous thromboembolism were assessed and aspirin was deemed inappropriate in 22 patients. The provider agreed with deprescribing aspirin therapy in 45 %. The most common dose and indication of aspirin therapy was 81 mg (98 %) and primary prevention (40 %) respectively.
Conclusions: In our small practice, pharmacist-led interventions were an effective means to recommend aspirin discontinuation in our identified patients. Further studies are needed to optimize a pharmacist's role and address the long-term effects of deprescription.

1. Introduction

Aspirin has been widely used for over one hundred years largely due to its antiplatelet (APT) properties. Benefits of aspirin therapy for secondary prevention of cardiovascular (CV) event recurrence is well established and societal treatment guidelines continue to recommend its use in persons with a history of myocardial infarction (MI), transient ischemic attack (TIA), cerebrovascular accident (CVA), and other classified acute coronary syndrome (ACS) events [1–3].

Aspirin duration of use for secondary prevention has been further evaluated in patients who received percutaneous coronary intervention (PCI) or coronary artery bypass graft surgery (CABG) in patients receiving oral anticoagulant (OAC) therapy. The AFIRE trial compared the efficacy and safety of rivaroxaban monotherapy vs. rivaroxaban and an APT (e.g., either aspirin or a P2Y12 inhibitor) combination therapy in patients with atrial fibrillation (AF) who had undergone PCI or CABG more than one year prior to study initiation [4]. The primary efficacy outcome was the composite of CVA, systemic embolism, MI, unstable angina requiring revascularization, or death from any cause and the safety outcome was major bleeding. Rivaroxaban monotherapy exhibited noninferiority to rivaroxaban and APT combination therapy in the primary efficacy outcome [hazard ratio (HR) 0.72; 95 % confidence

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interval (CI) 0.55–0.95; $P < 0.001$]. For the safety outcome, rivaroxaban monotherapy was superior to combination therapy [HR 0.59; 95 % CI 0.39–0.89; $P = 0.01$]. The 2020 ACC Expert Consensus Decision Pathway provides estimations of a ≥20 to 60 % increased risk of bleeding when APT therapy is added to OAC therapy, and that adding an additional APT further increases the risk 2- to 3-fold. Because of the bleeding and efficacy data available, current expert consensus statements recommend limiting the dose and length of antiplatelet therapy, including aspirin, for patients with AF or venous thromboembolism (VTE) undergoing PCI or CABG to one year for most patients [5].

Although aspirin use for secondary prevention of CV event recurrence and limited duration of use in patients post PCI or CABG is supported in literature, its risk of bleeding may be greater than its benefit in other clinical indications. In particular, aspirin for primary prevention of CV events has been shown to offer little benefit while increasing the risk of bleeding. Three randomized trials including ARRIVE, ASCEND, and ASPREE assessed aspirin therapy for primary prevention in patients with moderate risk of CV events, patients with diabetes, and in patients 70 years of age and older, respectively [6–8]. Each study demonstrated limited to no benefit of aspirin therapy in reducing CV events but increased bleeding risk. ORBIT-AF trial provided additional insights on the benefits and risks of aspirin therapy in patients with AF receiving OAC therapy [9]. After baseline characteristics adjustments, major bleeding and hospitalization due to bleeding were more likely in patients receiving the combination of OAC and aspirin compared to OAC alone. Additionally, many patients take aspirin for primary prevention without their provider's knowledge. The 2017 National Health Institutes Survey found that 23.4 % of adults in the U.S. aged 40 years or older, without CV disease, were taking aspirin as primary prevention to reduce the risk of CV disease (approximately 29 million persons) [10]. Of these patients, one out of four used aspirin without a physician's recommendation (approximately 6.6 million persons). In early 2022, the U.S. Preventive Services Task Force (USPSTF) released the revised recommendation statement on aspirin use to prevent CVD and CVA after extensive review of evidence [11]. For those aged 60 or older without a history of CV disease, the USPSTF now recommends against initiating aspirin for primary prevention due to the risk of bleeding outweighing benefit. This recommendation also supports deprescribing aspirin in this patient population.

Pharmacists can play a meaningful role to reduce the number of patients on inappropriate combined APT and anticoagulant therapy. A recent study showed positive impact of pharmacist interventions to identify and reduce inappropriate antithrombotic therapy in a large patient care setting, but mores studies are needed to recognize the prevalent inappropriate aspirin therapy and to develop an effective deprescribing process in various patient care settings [12]. This present study describes a pharmacist-led process to identify and discontinue inappropriate aspirin use in outpatient anticoagulation clinic patients in a small community hospital and the effectiveness of the interventions.

2. Materials and methods

This is a quality improvement initiative performed in an outpatient anticoagulation clinic in a small community hospital (Mercy Health - St. Anne Hospital, Toledo, Ohio) with approximately 270 enrolled patients. Certified anticoagulation care provider (CACP) pharmacists provide 40 h of service per week. The clinic primarily manages warfarin therapy, though services are available to patients taking direct-acting oral anticoagulants (DOACs) as well. During routine visits, anticoagulation clinic pharmacists review all medications with patients utilizing the electronic medical record (EMR) medication list as standard of care. Between October 7, 2021, and January 5, 2022, the clinic implemented a process to identify and recommend deprescription of inappropriate aspirin therapy. Pharmacists specifically asked patients if they take daily aspirin, regardless of the presence or absence of aspirin on their medication list. This was intended to identify those who were taking aspirin without the recommendation of a provider. If the patient stated they did take daily aspirin, the medication list was updated. For all patients who confirmed aspirin use, the pharmacist conducted a patient interview and chart review utilizing the EMR to obtain necessary data to identify those on inappropriate aspirin therapy. Data was initially recorded on paper using the Anticoagulant & Antiplatelet Therapy Evaluation Form (Appendix 1). The following data was prospectively collected during routine clinic appointments: anticoagulant agent (warfarin or DOAC), indication, and estimated duration of therapy, dose and indication of aspirin therapy, and demographic information including age and sex. For any remaining data not collected during the appointment, a chart review was conducted to complete the evaluation form. Patient data from the evaluation forms was then transferred and compiled to an encrypted electronic spreadsheet. If a patient had multiple appointments during the study's timeframe, they were only assessed for aspirin deprescription once.

Patients ≥40 years old on indefinite anticoagulation therapy for AF or VTE were further assessed for inappropriate aspirin therapy. Patients on anticoagulation for indications other than AF or VTE were excluded. The aspirin indication was categorized as primary prevention, secondary prevention, post-CABG, or post-PCI. Because of the inherent increased bleeding risk associated with anticoagulants, all clinic patients using aspirin for primary prevention were candidates for aspirin deprescription. For secondary prevention, aspirin therapy was deemed appropriate, and no further evaluation was conducted. For post-CABG or post-PCI indication, the time elapsed since the procedure was evaluated to determine appropriateness of aspirin therapy. Patients who were on aspirin longer than the recommended duration by the Expert Consensus of the American College of Cardiology were identified as taking inappropriate aspirin therapy [8]. For CABG, the recommendation is to use aspirin for one year. For bare metal stents aspirin therapy is not recommended. For post-PCI with a drug-eluting stent (DES), the recommendation is to use a P2Y12-inibitor for six months followed by aspirin or P2Y12-inhibitor for an additional 6–12 months. To be conservative we chose >18 months as the inappropriate aspirin duration for post-PCI with DES.

Following the evaluation of each patient, if inappropriate aspirin therapy was identified, the Aspirin Deprescription Recommendation Form (Appendix 2) was faxed to the provider. If no response was obtained from the provider five business days after the initial faxed communication, a phone call to the provider's office was made to confirm the correct fax number and if the fax was received. If voicemail was reached, a message was left requesting confirmation that the fax was received. If receipt of initial fax was unconfirmed, the form was refaxed one additional time. Faxed provider responses were recorded as accepted, rejected, or no response. “Accepted” response was defined as provider stating “Yes” to deprescribing aspirin therapy, and “Rejected” response was defined as provider stating “No” to deprescribing aspirin therapy. If the recommendation was “Rejected”, the provider was asked to indicate the reason for aspirin continuation by selecting one of the following choices: benefit outweighs risk, patient preference, or other (please specify). “No Response” was defined as no response after 5 business days from the second faxed communication. If an “Accepted” response was received, the clinic pharmacist contacted patients by phone to communicate instruction to discontinue aspirin therapy. Questions from the patient were answered, and a note to follow up at the next anticoagulation clinic appointment was made to ensure the patient was no longer taking aspirin and to address any patient concerns.

Outcome data was retrospectively collected to assess the effectiveness of pharmacist-led intervention. The primary outcome of this study was the percentage of “Accepted” recommendations. Secondary outcomes included the prevalence of anticoagulation clinic patients on aspirin therapy and the indications for aspirin use. Descriptive statistics were used for all results. Because this study reports the results of a quality-improvement initiative, the institutional Investigational Review Board (IRB) did not require a formal review.

3. Results

Between October 7, 2021, and January 5, 2022, a total of 242 patients completed one or more visits within our anticoagulation clinic and 80 patients (33 %) were on concurrent aspirin therapy. Of those, 52 patients had AF or VTE indication and were assessed for aspirin appropriateness. Table 1 displays patient demographics, type of anticoagulation therapy, and indication for aspirin. The mean age was 72.7 years and 65 % were male. Warfarin (98 %) was the most common type of anticoagulant therapy. The most common daily dose of aspirin was 81 mg (98 %) with only one patient taking 325 mg. The most common indications for aspirin therapy included primary prevention (40 %), CVA (19 %), and peripheral vascular disease with or without claudication (13 %).

Upon assessment by the pharmacist, combined aspirin and anticoagulation therapy were deemed appropriate in 30 out of 52 patients, requiring no further action. The remaining 22 patients were considered eligible for possible aspirin deprescription, with the indications of primary prevention ($n = 21$) or prolonged (>18 months) combined therapy following PCI ($n = 1$).

Fig. 1 details pharmacists' deprescription interventions and outcomes. Of the 22 pharmacist recommendations to deprescribe aspirin, a reply was received for 15, demonstrating a 68 % response rate. Of the 15 responses, the provider agreed to discontinue aspirin therapy in 10 patients (67 % approval rate). For the six patients with VTE as their anticoagulation indication, 100 % of the recommendations were accepted. Two recommendations were rejected with the reason of "benefit outweighs risk." One recommendation was rejected due to a secondary prevention indication that was missed upon chart review. Two provider responses did not specify a reason for continuing aspirin.

Table 1
Characteristics of AF & VTE patients on aspirin & anticoagulant therapy.

	Total patients	Appropriate aspirin therapy	
	52	Yes (n = 30)	No (n = 22)
Baseline characteristics			
Age (years; mean ± SD)	72.7 ± 8	72.9 ± 8	72.6 ± 8
Female, no. (%)	18 (34 %)	12 (40 %)	6 (27 %)
Type of anticoagulation therapy			
Warfarin	51 (98 %)	29 (97 %)	22 (100 %)
Direct-acting oral anticoagulants	1 (2 %)	1 (3 %)	0 (0 %)
Indication for anticoagulation - no. (%)			
Nonvalvular atrial fibrillation	42 (81 %)	26 (87 %)	16 (73 %)
Venous thromboembolism	10 (19 %)	4 (13 %)	6 (27 %)
Strength of aspirin – no. (%)			
81 mg	51 (98 %)	29 (97 %)	22 (100 %)
162 mg	0 (0 %)	0 (0 %)	0 (0 %)
325 mg	1 (2 %)	1 (3 %)	0 (0 %)
Indication[a] for antiplatelet - no. (%)			
Primary prevention	21 (40 %)	0 (0 %)	21 (95 %)
CVA	10 (19 %)	10 (33 %)	0 (0 %)
TIA	1 (2 %)	1 (3 %)	0 (0 %)
CAD with stable angina	6 (12 %)	6 (20 %)	0 (0 %)
Acute coronary syndrome	6 (12 %)	6 (20 %)	0 (0 %)
Coronary or other arterial revascularization	1 (2 %)	1 (3 %)	0 (0 %)
Peripheral vascular disease	7 (13 %)	7 (23 %)	0 (0 %)
Aortic aneurysm	2 (4 %)	2 (7 %)	0 (0 %)
Post-PCI	1 (2 %)	0 (0 %)	1 (5 %)
Post-CABG	0 (0 %)	0 (0 %)	0 (0 %)

CVA- cerebrovascular accident; TIA- transient ischemic attack; CAD- coronary artery disease; PCI- percutaneous coronary intervention; CABG- coronary artery bypass graft surgery.

[a] Indications may be greater than total due to patient's having more than one indication.

4. Discussion

Concurrent use of aspirin and indefinite OAC therapy pose an increased bleeding risk to patients with minimal prevention of CV events [13,14]. Our study found that aspirin use is prevalent (33 %) among outpatient anticoagulation clinic patients and a substantial proportion (28 %) of those aspirin users was potentially eligible for deprescription with primary prevention being the most common indication. Our pharmacist-led intervention was effective not only to identify inappropriate aspirin therapy, but also led to relatively high aspirin discontinuation rate (10/22; 45 %). In a typical anticoagulation clinic without a deprescription protocol, the discontinuation of inappropriate aspirin may not occur. The successful deprescribing rate in our study may be explained by the positive working relationship built on trust we have acquired with area providers as well as our patients. Deprescribing a medication requires approval from both providers and patients. Patients are hypothetically willing to have a medication deprescribed, but some barriers including perceived benefit of the medication, fear of being without the medication, and recommendation of their provider may hinder them from discontinuing a medication [15]. In our study, pharmacists had meaningful conversations with patients, conveying their providers' approval of aspirin discontinuation and addressing their concerns. Consequently, all discontinuations were accepted by the patients.

The impact of our pharmacist-led interventions may be extended beyond the reported response rate as we provided education and facilitated patient-provider conversations. For example, a cardiologist who was faxed with our recommendation to deprescribe aspirin did not formally respond to us via fax but communicated this to the patient. This patient did not count as an "accepted response" in our study, but the intervention led to provider's recognition of inappropriate aspirin therapy and subsequent discontinuation.

Meador and colleagues recently reported a successful outcome of their pharmacist-driven interventions to identify and de-escalate inappropriate combined APT (i.e. aspirin and/or clopidogrel) and anticoagulation therapy within an outpatient antithrombotic clinic in a large academic medical center [12]. Of 875 included patients in their study, 261 (30 %) were on combined antiplatelet and anticoagulant therapy and 48 (18 %) of those were deemed inappropriate combined therapy. Pharmacist-driven efforts were highly effective resulting in de-escalation of inappropriate combined therapy in 43 (93 %) patients. Meador et al. had a different study design and setting, it would be difficult to directly compare our findings to theirs. However, both studies show that concurrent aspirin use is prevalent (33 % in our study and 30 % in Meador et al.) among patients receiving chronic anticoagulation therapy and an opportunity exists for aspirin deprescribing. Interestingly, Meador et al. reports much higher de-escalation rate (93 %) following pharmacist-interventions compared to our deprescribing rate (45 %). It should be noted that de-escalation in their study included aspirin dose reduction, switching clopidogrel to aspirin as well as aspirin deprescription. More importantly, pharmacists in their study were allowed to deprescribe inappropriate combined antithrombotic therapy autonomously and about 30 % of inappropriate therapy was de-escalated by pharmacists. Pharmacist's direct communication with providers might also contribute to a higher provider response rate (95 % vs. 68 % in our study) and subsequently a high de-escalation rate. Aspirin discontinuation with the provider's agreement accounts for ~60 % of all de-escalation cases in their study, which may be comparable to our results.

Some factors could have impacted on our deprescribing rate. Our clinic utilizes faxing as our primary provider communication method because a significant portion of our referring providers do not utilize our health system's EMR. Patients are referred to our anticoagulation clinic occasionally upon discharge from our hospital or through the existing relationship with area providers from different health systems. Unfortunately, providers often have full schedules with little time to address

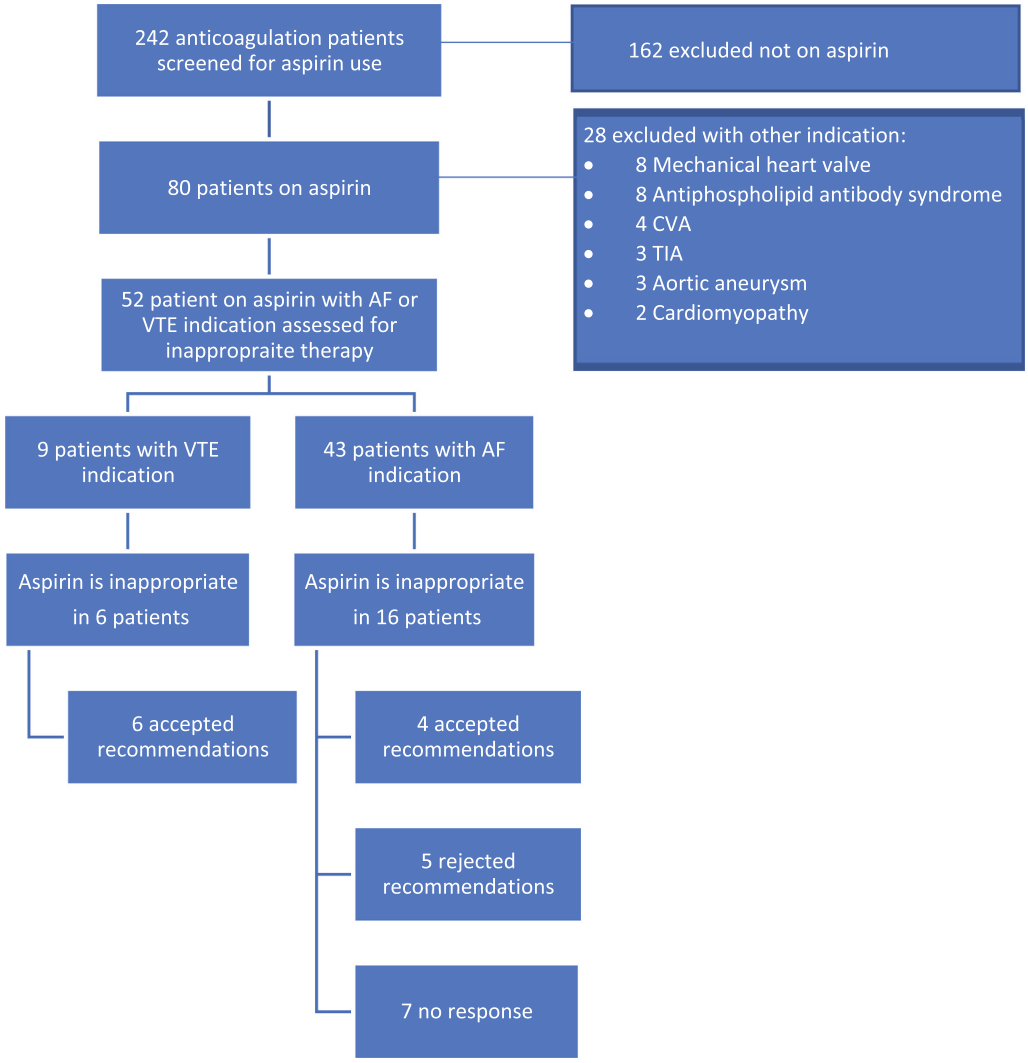

Fig. 1. Details of pharmacist-led intervention to deprescribe inappropriate aspirin therapy.

daily faxes in a timely manner, potentially affecting the response rate. Providers are logged on to an EMR for significant portion of the day. One study of primary care physicians found that 4.5 h was spent working in the EMR with an additional 1.4 EMR hours spent outside of the scheduled clinic hours [16]. It is possible that our response rates may have been higher if we utilized EMR messaging system for providers that share our EMR. Another challenge encountered in our process was to select the provider to communicate with regarding potentially inappropriate aspirin therapy and deprescribing opportunity. For example, one cardiologist felt uncomfortable deprescribing aspirin therapy because the patient was not seen in three years. The patient's primary care provider was then faxed and agreed with aspirin deprescription. Other providers may have chosen not to respond due to similar concerns. Our fax form may benefit from the addition of adding a selection to defer decision to a specialist such as cardiologist or hematologist. Finally, during our study period, the draft of the aforementioned USPTF recommendation statement was released increasing the awareness of this topic and may have impacted on our study [11]. For example, a few of our clinic patients decided to self-discontinue aspirin therapy prior to being evaluated during our study which reduced the number of pharmacist interventions.

Although our clinic is small in size, serving <300 patients, we were able to complete a meaningful quality improvement project to help deprescribe inappropriate aspirin therapy. In large academic medical centers, multiple pharmacists and resources may be available daily to perform various clinical services. In our clinic, we rarely have more than one pharmacist staffing the clinic at a time, but we were able to easily integrate this process into our workflow with minimal time commitment. Initial data collection with the evaluation form took no more than 2 additional minutes from the scheduled 15-minute anticoagulation appointment. Chart review using the EMR to complete the evaluation form took approximately 5 min. When inappropriate aspirin use was identified, time to fax the provider, assess provider responses and follow up patients could take an additional 10–15 min per patient. During the study period, a pharmacist typically spent an additional 1 h per week to complete all chart review, faxing, and patient contacts pending approval from the provider. Implementing a similar deprescription effort may be feasible in other patient care settings. Community pharmacies may adapt our process with the evaluation and provider fax forms to assess inappropriate aspirin and communicate deprescription recommendations. The provider response may be lower due to less personal relationships, however, engaging the patients with the intervention may help build the patient-pharmacist relationship and assist patients with initiating conversations with their providers.

Our study has several limitations. First, we did not evaluate any important safety outcomes such as CV events or bleeding. Future studies could add to the evidence supporting the benefits of aspirin deprescription. Additionally, our standardized evaluation form may have been too simplified to correctly identify all inappropriate aspirin indications; however, the form was practical for our pharmacists to use and easily

identify deprescribing opportunities. Although overall the form helped capture those with clear inappropriate indications during chart review, one patient was incorrectly categorized by the pharmacist as primary prevention when there was a remote history of MI listed in the EMR (the provider noted this and sent a "rejected" response). Other pertinent medical history may also be difficult to obtain for provider offices utilizing other EMRs.

5. Conclusions

Our study showed that pharmacist-led interventions using a simple evaluation form can assist to identify inappropriate aspirin therapy among patients in an anticoagulation clinic and reduce the number of patients with inappropriate aspirin therapy. Further studies can inform to optimize pharmacist-led, targeted aspirin deprescription efforts to benefit patients in different practice settings.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

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