



Letter to the Editors-in-Chief

Anticoagulation and antiplatelet therapy in stable coronary artery disease: A multicenter survey



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1. Introduction

Oral anticoagulation (OAC) is superior to antiplatelet therapy to prevent stroke in patients with atrial fibrillation (AF). In contrast, patients who have experienced an acute coronary event and/or coronary stent placement benefit from antiplatelet therapy to prevent future adverse cardiac events. While both of these cardiac conditions are highly prevalent on their own, they also frequently occur concurrently. In these situations, combined antiplatelet therapy and OAC significantly increases the risk of bleeding events [1,2]. Several randomized controlled trials over the past decade have tried to identify a safe and effective antithrombotic regimen for patients with AF who undergo coronary stent placement. However, an optimal antithrombotic regimen for patients with AF who have stable coronary artery disease (CAD) (> 12 months from the last coronary event) is unknown. To investigate how clinicians manage antithrombotic medications in patients with comorbid AF and stable CAD in contemporary practice, we conducted a multicenter survey of cardiologists at academic and private health systems.

2. Methods

Between August 27, 2018, and September 22, 2018, we invited cardiologists at three health centers (the University of Michigan, Duke University, and Piedmont Healthcare) to participate in an online survey. Clinicians were presented with several different hypothetical scenarios of patients with CAD and AF who were at an elevated stroke risk in which they had to select the use of OAC and/or aspirin. The scenarios varied by the type of coronary syndrome leading to the initial stent placement (acute coronary syndrome or stable angina) and time since stent placement (1 or 3 years ago). One scenario included a patient with a history of peptic ulcer bleed and one scenario included a patient that did not have any known CAD or history of intervention (Fig. 1). Clinician practice and training descriptions were also obtained. The complete survey is available in the supplementary appendix. Survey response frequencies are reported and statistical association measured using McNemar's chi-squared test for paired data (Stata, Version 14.2). This study was deemed exempt by the institutional review board at the University of Michigan; consent was implied through participation in the optional survey.

3. Results

A total of 49/149 (32.9%) clinicians completed the survey. Noninvasive cardiologists comprised about half of the participants (23, 46.9%) while invasive cardiologists (12, 24.5%) and electrophysiologists (9, 18.4%) were the next most common. Most clinicians were men (40, 81.6%) and from an academic medical center (39, 79.6%). There was a wide range of years in practice with clinicians' completion of training spanning from 1970 to 2018 (median 2007). Survey respondents spent the majority of their work week time in direct patient care (median 75%, interquartile range 50–90%).

There was wide consensus regarding the use of OAC in patients with AF and elevated stroke risk and > 99% (342/343 total selections across all vignettes) of respondents favored its use across all scenarios. The use of aspirin in addition to OAC in the setting of CAD was variable. In patients with coronary stent placement 1 year prior for stable angina, 35/48 (72.9%) chose to continue aspirin which decreases to 27/48 (56.3%) after 3 years ($p = 0.008$). In patients with coronary stent placement 1 year prior for a non-ST segment elevation myocardial infarction (NSTEMI), 40/48 (83.3%) chose to continue aspirin which decreases to 32/49 (65.3%) after 3 years ($p = 0.004$). In patients with recent coronary stent placement for a NSTEMI 3 months ago already on OAC and clopidogrel, 7/46 (15.2%) also chose additional aspirin. With respect to primary prevention, 5/45 (11.1%) favored aspirin use in patients already on OAC. The use of a proton pump inhibitor (PPI) to reduce bleeding risk was rare with only 4.4%–15.6% of clinicians favoring its use across all vignettes excluding one vignette with peptic ulcer disease where 45/49 (91.8%) favored PPI use. In patients with concurrent CAD using aspirin and AF, responding cardiologists preferred full dose (as compared to reduced dose) direct oral anticoagulants (45/48, 93.8%).

4. Discussion

Our study has three major findings. First, the majority of clinicians favored the use of aspirin in patients with AF on OAC, even with “stable CAD” at 1 and 3 years following stent placement. Second, both the time from stent placement and the type of CAD presentation (stable angina vs NSTEMI) appear to influence a clinician's decision-making when determining the length of aspirin treatment in patients with AF on OAC.

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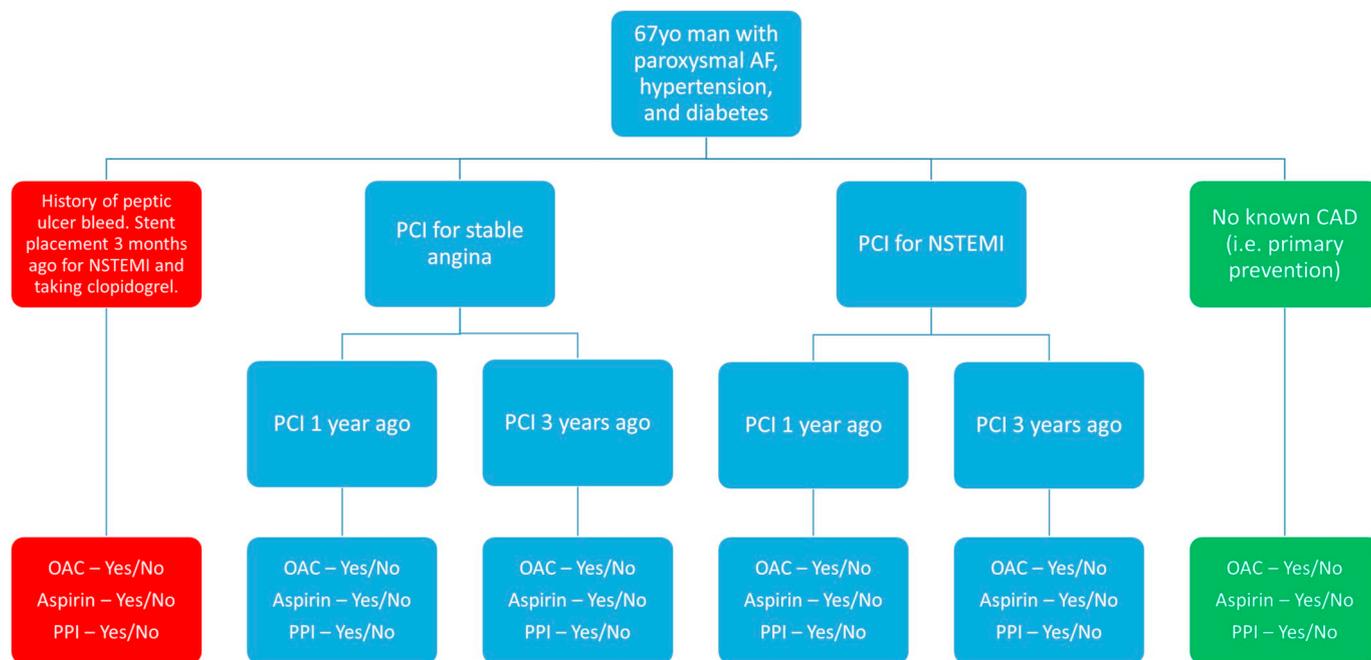


Fig. 1. Schematic representation of survey questions. Flow chart representation of survey questions. Abbreviations: AF = atrial fibrillation, CAD = coronary artery disease, NSTEMI = non-ST segment elevation myocardial infarction, OAC = oral anticoagulation PCI = percutaneous coronary intervention, PPI = proton pump inhibitor, yo = year old.

Lastly, PPI use is infrequently utilized even in scenarios where multiple antithrombotic agents are being used.

There is no clear consensus across US and European guidelines regarding antiplatelet therapy in patients with AF on OAC and stable CAD. Our survey results suggest that the majority of cardiologists favor continuing both OAC and antiplatelet therapy in patients with stable CAD and AF. Technically, this is congruent with the most recent North American guidelines. The American Heart Association (AHA)/American College of Cardiology (ACC)/Heart Rhythm Society (HRS) AF guidelines from 2014 (including a 2019 focused update) make no specific recommendation regarding aspirin use in patients with AF on OAC and stable CAD [3,4]. This combined with the recommendation from the AHA/ACC guidelines for stable CAD for indefinite aspirin use in patients with stable CAD has led to the common practice of continuing both OAC and antiplatelet therapy [5]. However, there is mounting evidence to suggest that OAC monotherapy provides similar protection against coronary events with less bleeding as compared to OAC + antiplatelet therapy in patients with stable CAD [2]. The largest cohort, reported by Lamberts et al. [2], found that in patients with stable coronary disease the addition of aspirin to OAC resulted in a similar risk of MI/coronary death compared with OAC monotherapy, but carried with it a significantly increased risk of bleeding (hazard ratio 1.50; 95% CI, 1.23–1.82). This evidence is reflected in recent CHEST guidelines and a 2018 Joint European consensus document on antithrombotic therapy in AF endorsed by the HRS which both recommend OAC alone in patients > 12 months from either an acute coronary event and/or stent placement [6,7]. Similar recommendations are made by North American experts on the topic in a 2016 document with an update published in 2018 [8]. This survey suggests that these newer recommendations are not widely practiced. Clearly, there will be situations in which indefinite aspirin in addition to OAC may be appropriate (high risk coronary stents, high residual ischemic burden, history of frequent recurrent cardiac events, etc.), but these cases are less common and could be handled on an individual basis.

Our survey suggests that there were some instances in which clinicians were more likely to pursue OAC monotherapy. The time from the last coronary event was important as after elective PCI, 72.9% favored

aspirin at 1 year and 56.3% favored it at 3 years. The type of event leading to stent placement was also important as at 1 year, 72.9% favored aspirin after elective PCI and 83.3% favored it after PCI for a NSTEMI. In the absence of known CAD, only 11.1% favored the use of aspirin which is in concordance with data from several recent randomized trials regarding aspirin for primary prevention of CAD [9].

Lastly, the choice to use a PPI was infrequently selected in the survey. Despite the use of multiple antithrombotic agents, a minority of clinicians consistently favored PPI use. The only exception to this was in one scenario where the vignette included a history of peptic ulcer disease and gastrointestinal bleeding in which the majority of clinicians favored PPI use. These results are somewhat surprising as PPIs are an effective strategy to reduce bleeding in patients on OAC and/or aspirin and the majority of patients were actually on both [10]. PPIs are usually preferred to H2-receptor antagonists to prevent bleeding in the setting of antiplatelet and/or OAC use, although research comparing the two in this setting is lacking.

We recognize limitations in our study, including a relatively small sample size of cardiologists from three centers, which could limit generalizability. However, these clinicians represent three specialties within academic and non-academic cardiology practices across the Midwest and Southern regions of the United States.

Overall, our survey suggests that the concomitant use of aspirin and OAC in patients with AF and stable CAD is high. Current evidence suggests that this strategy is unlikely to reduce ischemic events and increases bleeding events. We agree with the aforementioned recent guideline recommendations to pursue OAC monotherapy in stable CAD > 12 months after a coronary event or stent placement. Incorporating these recommendations into practice may represent an opportunity for patient care improvement.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.thromres.2019.05.017>.

References

- [1] M.L. Hansen, et al., Risk of bleeding with single, dual, or triple therapy with warfarin, aspirin, and clopidogrel in patients with atrial fibrillation, *Arch. Intern. Med.* 170 (2010) 1433–1441.
- [2] M. Lamberts, et al., Antiplatelet therapy for stable coronary artery disease in atrial fibrillation patients taking an oral anticoagulant: a nationwide cohort study, *Circulation* 129 (2014) 1577–1585.
- [3] C.T. January, et al., 2014 AHA/ACC/HRS guideline for the management of patients with atrial fibrillation: a report of the American College of Cardiology/American Heart Association Task Force on practice guidelines and the Heart Rhythm Society, *Circulation* 130 (2014) e199–e267.
- [4] C.T. January, et al., AHA/ACC/HRS focused update of the 2014 AHA/ACC/HRS guideline for the management of patients with atrial fibrillation, *Circulation* 2019 (2019) CIR0000000000000665.
- [5] S.D. Fihn, et al., 2012 ACCF/AHA/ACP/AATS/PCNA/SCAI/STS guideline for the diagnosis and management of patients with stable ischemic heart disease: a report of the American College of Cardiology Foundation/American Heart Association task force on practice guidelines, and the American College of Physicians, American Association for Thoracic Surgery, Preventive Cardiovascular Nurses Association, Society for Cardiovascular Angiography and Interventions, and Society of Thoracic Surgeons, *Circulation* 126 (2012) e354–e471.
- [6] G.Y.H. Lip, et al., Antithrombotic therapy for atrial fibrillation: CHEST guideline and expert panel report, *Chest* 154 (2018) 1121–1201.
- [7] G.Y.H. Lip, et al., 2018 Joint European consensus document on the management of antithrombotic therapy in atrial fibrillation patients presenting with acute coronary syndrome and/or undergoing percutaneous cardiovascular interventions: a joint consensus document of the European Heart Rhythm Association (EHRA), European Society of Cardiology Working Group on Thrombosis, European Association of Percutaneous Cardiovascular Interventions (EAPCI), and European Association of Acute Cardiac Care (ACCA) endorsed by the Heart Rhythm Society (HRS), Asia-Pacific Heart Rhythm Society (APHRS), Latin America Heart Rhythm Society (LAHRS), and Cardiac Arrhythmia Society of Southern Africa (CASSA), *Europace* 21 (2) (2019) 192–193, <https://doi.org/10.1093/europace/euy174> (Feb 1).
- [8] D.J. Angiolillo, et al., Antithrombotic therapy in patients with atrial fibrillation treated with oral anticoagulation undergoing percutaneous coronary intervention, *Circulation* 138 (2018) 527–536.
- [9] J.M. Gaziano, et al., Use of aspirin to reduce risk of initial vascular events in patients at moderate risk of cardiovascular disease (ARRIVE): a randomised, double-blind, placebo-controlled trial, *Lancet* 392 (2018) 1036–1046.
- [10] W.A. Ray, et al., Association of oral anticoagulants and proton pump inhibitor co-therapy with hospitalization for upper gastrointestinal tract bleeding, *Jama* 320 (2018) 2221–2230.

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