Underuse of anticoagulation therapy for atrial fibrillation

Are we failing our patients?

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Mavis is 78 years old and fiercely independent. She lives alone but has an active social life, particularly enjoying the Friday tea dance at her local village hall. She has high blood pressure and diabetes, which are both well controlled with oral medication. At Mavis' annual blood pressure review, the nurse detects an irregularly irregular pulse and electrocardiogram results confirm atrial fibrillation (AF) at a rate of 74 beats per minute. Mavis sees her GP. He asks her if she experiences palpitations, shortness of breath, or chest pain. Mavis has not noticed any symptoms at all. Her GP reassures her that this is just an incidental finding and nothing more needs to be done. Three months later, Mavis is admitted to hospital with slurred speech and a sudden weakness in her left arm and leg. A computed tomographic scan confirms a large infarct in the right parietal lobe. Despite physiotherapy, she requires help to mobilize with a walking aid and to get to the toilet. She is discharged to a nursing home 1 month after admission.

Atrial fibrillation affects up to 33.5 million people worldwide and is associated with considerable adverse outcomes including a 5-fold increased risk of stroke.[1] Prospective risk of stroke can be estimated using a validated scoring system, such as the CHA_2DS_2-VASc (congestive heart failure, hypertension, age ≥75 years, diabetes mellitus, stroke or transient ischemic attack, vascular disease [previous myocardial infarction, peripheral artery disease, or aortic plaque], age 65 to 74 years, sex category [ie, female]) model, which incorporates weighting for risk factors shown to correlate with stroke. If used appropriately in people with AF and high risk of stroke (ie, a CHA_2DS_2-VASc score of ≥ 2), anticoagulation therapy with either a vitamin K antagonist or direct oral anticoagulant can reduce risk of stroke by 64% compared with placebo.[2,3] For low- or moderate-risk patients (ie, a CHA_2DS_2-VASc score of 0 or 1), the potential harm of bleeding outweighs or is similar to the benefit of anticoagulation therapy. Given that Mavis is older than age 75 (2 points) and a woman with hypertension and diabetes (1 point each), her CHA_2DS_2-VASc score is 5.

This evidence is not new yet international anticoagulation prescribing rates remain low. A 2010 systematic review found that in more than two-thirds of the 54 included studies, less than 60% of patients at high risk of stroke were treated with anticoagulation therapy.[4] In a 2015 UK retrospective observational cohort study that included 2259 participants with AF, who were identified from primary care databases using the GRASP-AF (Guidance on Risk Assessment and Stroke Prevention in AF) tool, 85.6% had a CHA_2DS_2-VASc score of 2 or higher. In this high-risk group, 39.7% of participants were not receiving anticoagulation therapy and more than a third were inappropriately receiving antiplatelet monotherapy.[5] A retrospective analysis of 29 043 UK patients with a first-ever stroke or transient ischemic attack found 52% (1647 of 3194) of those known to have had AF before the event had not been prescribed prophylactic anticoagulation therapy when clinically indicated.[6]

A fundamental principle of medical ethics is "First, do no harm." Acting in nonmaleficence, we might be reluctant to initiate anticoagulation therapy owing to the risk of bleeding. In a survey of 596 GPs, 17.6% of respondents anticipated feeling responsible if they had started a patient on anticoagulation therapy and then the patient had a subsequent intracranial hemorrhage (ICH).[7] The responsibility physicians feel when adverse events occur affects prescribing and changes practice; when a physician has a patient who experiences an adverse bleeding event while taking anticoagulants, there is a 21% reduction in the odds of him or her prescribing anticoagulation therapy to subsequent patients in the next 90 days.[8] However, when a patient who does not take anticoagulants has a stroke, there is no relevant change in subsequent physician prescribing.[8] It seems we feel more responsible when a treatment we have initiated results in harm than when we have chosen not to intervene, even though there might be a greater risk of indirect harm and similarly serious consequences.

We tend to overestimate the risks of anticoagulation therapy in patients with comorbidities, such as recurrent falls or previous peptic ulcer. In a small qualitative study involving 14 senior physicians, all participants given case

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vignettes chose not to start anticoagulation therapy in an elderly patient, despite her 1-year stroke risk of 18%, owing to her history of recurrent falls and concerns about causing ICH.[9] Yet a Markov decision analytical model suggested that a patient taking anticoagulants would have to fall more than 294 times in a single year before the risk of ICH outweighed the benefit of treatment, and, indeed, risk of falls does not feature on the HAS-BLED (hypertension with a systolic blood pressure >160 mm Hg, abnormal renal or liver function, stroke [caused by bleeding], bleeding, labile international normalized ratio, elderly [age >65 y], drugs [acetylsalicylic acid or nonsteroidal anti-inflammatory drugs] or alcohol [≥8 drinks/wk]) risk of bleeding scoring system.[10] Furthermore, if ICH is a considerable concern, the already low risk of ICH with warfarin is reduced by at least 50% with direct oral anticoagulants. The 2016 European Society of Cardiology guidelines on the management of AF state the following: "A high bleeding risk score should generally not result in withholding oral anticoagulation. Rather, bleeding risk factors should be identified and treatable factors corrected."[11] We believe we are acting with beneficence in protecting patients from the risks of anticoagulation therapy, but unless we are objectively balancing both their bleeding and stroke risk simultaneously, we are not making an evidence-based decision.

The variation in treatment decisions means there is unjustified variation of care for patients; the individual GP that a patient with AF sees might be just as important in determining if anticoagulation is initiated as the patient's overall stroke risk. This type of disparity exists in many areas of medicine but rarely when the benefits of treatment are so well established. Such variation also affects the wider community. Strokes in association with AF are larger, more disabling, and have a higher cost at every time point after the event. Mavis went from independent living to nursing home placement following her stroke, and patients with disabling stroke often require additional nursing, therapy, and social care, as well as family support, which can have both psychological and financial implications.

Physicians frequently cite patient preference when anticoagulation therapy has not been started. However, we might not be providing the correct information for patients to make an informed decision if we struggle to fully understand and objectively weigh this complex balance of risks and benefits ourselves. Are we presenting information on risks and benefits in an easily understandable way, free from our own subjectivity to allow patients to meaningfully participate in decision making? As these decisions become more complex in an aging population, with more comorbidities, polypharmacy, and more anticoagulant treatment options available, is it appropriate that we tend to err on the side of perceived caution by choosing not to add in further medication with well documented risks? Often in medicine controversy lies in overmedicating and pressure to introduce new treatment options where the benefits are not established. Anticoagulation is an example of an extremely cost-effective treatment that is being underused resulting in harm to patients, their families, and the wider community partly because of physicians' and patients' concerns about its risk profile. We must get better at recognizing that decisions to not treat patients can result in considerable indirect harm, and so balance these risks against the potential direct harms from treatment. This is particularly important where the risk-benefit balance is so skewed toward benefit, as in not prescribing anticoagulation therapy for AF when the risk of stroke is high.

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Competing interests

None declared

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References

1. Wolf PA, Abbott RD, Kannel WB. Atrial fibrillation as an independent risk factor for stroke: the Framingham study. *Stroke* 1991;22(8):983-8.
2. Hart RG, Pearce LA, Aguilar MI. Meta-analysis: antithrombotic therapy to prevent stroke in patients who have nonvalvular atrial fibrillation. *Ann Intern Med* 2007;146(12):857-67.
3. Hanley CM, Kowey PR. Are the novel anticoagulants better than warfarin for patients with atrial fibrillation? *J Thorac Dis* 2015;7(2):165-71.
4. Ogilvie IM, Newton N, Welner SA, Cowell W, Lip GY. Underuse of oral anticoagulants in atrial fibrillation: a systematic review. *Am J Med* 2010;123(7):638-45.
5. Shantsila E, Wolff A, Lip GY, Lane DA. Optimising stroke prevention in patients with atrial fibrillation: application of the GRASP-AF audit tool in a UK general practice cohort. *Br J Gen Pract* 2015;65(630):e16-23.
6. Turner GM, Calvert M, Feltham MG, Ryan R, Fitzmaurice D, Cheng KK, et al. Under-prescribing of prevention drugs and primary prevention of stroke and transient ischaemic attack in UK general practice: a retrospective analysis. *PLoS Med* 2016;13(11):e1002169.
7. Gattellari M, Worthington J, Zwar N, Middleton S. Barriers to the use of anticoagulation for nonvalvular atrial fibrillation: a representative survey of Australian family physicians. *Stroke* 2008;39(1):227-30. Epub 2007 Nov 29. Errata in: *Stroke* 2010;41(4):e398, *Stroke* 2008;39(4):e77.
8. Choudhry NK, Anderson GM, Laupacis A, Ross-Degnan D, Normand SL, Soumerai SB. Impact of adverse events on prescribing warfarin in patients with atrial fibrillation: matched pair analysis. *BMJ* 2006;332(7534):141-5. Epub 2006 Jan 10.
9. Anderson N, Fuller R, Dudley N. 'Rules of thumb' or reflective practice? Understanding senior physicians' decision-making about anti-thrombotic usage in atrial fibrillation. *QJM* 2007;100(5):263-9. Epub 2007 Mar 27.
10. Man-Son-Hing M, Nichol G, Lau A, Laupacis A. Choosing antithrombotic therapy for elderly patients with atrial fibrillation who are at risk for falls. *Arch Intern Med* 1999;159(7):677-85.
11. Kirchhof P, Benussi S, Kotecha D, Ahlsson A, Atar D, Casadei B, et al. 2016 ESC guidelines for the management of atrial fibrillation developed in collaboration with EACTS. *Eur Heart J* 2016;37(38):2893-962.

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