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Decision-making interventions to stop the global atrial fibrillation-related stroke tsunami

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Abstract

Atrial fibrillation affects 33.5 million people worldwide and its prevalence is expected to double by 2050 because of the aging population. Atrial fibrillation confers a 5-fold higher risk of ischemic stroke compared to sinus rhythm. We present our view of the role of shared medical decision-making to combat global underutilization of oral anticoagulation for stroke prevention in atrial fibrillation patients. Oral anticoagulation underuse is widespread as it is present within atrial fibrillation patients of all risk strata and in countries across all income levels. Reasons for oral anticoagulation underuse include but are probably not limited to poor risk stratification, over-interpretation of contraindications, and discordance between physician prescription preferences and actual administration. By comparing a catastrophic event to the consequences of atrial fibrillation related strokes, it may help physicians and patients understand the negative outcomes associated with oral anticoagulation under-utilization and the magnitude to which oral anticoagulations neutralize atrial fibrillation burden.

Keywords

Visual aid, framing, atrial fibrillation, stroke, oral anticoagulation, epidemiology

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Atrial fibrillation (AF) affects 33.5 million people worldwide[1] and its prevalence is expected to double by 2050 because of the aging population.[1] AF confers a 5-fold higher risk of ischemic stroke compared to sinus rhythm.[2] Relative to the ischemic strokes of other causes, AF-related strokes are usually larger[3] and more severe.[4,5] They also have greater recurrence,[6] disability,[3,5,7–9] and mortality[5,6,9,10] rates.

Shared medical decision-making is the practice by which the physician presents all possible alternatives to their patient, each with an associated risk/benefit trade-off.[11–14] This process incorporates patient values and preferences in their own health care decisions.[11–14] We present our view of the role of shared medical decision-making in stroke prevention for patients with AF, primarily through the administration of oral anticoagulants. Furthermore, the dangers of the inadequacies of stroke prevention in patients with AF are compared with a real-life natural catastrophe through the lens of the "flashbulb memory".

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Benefits of oral anticoagulants for AF patients

Compared to no treatment, warfarin reduces stroke risk by 64% and all-cause mortality by 26% in AF patients; in contrast, aspirin has a nonsignificant impact on stroke[15] and mortality.[16] Non-vitamin K antagonist oral anticoagulants (NOACs) further reduce the risk of stroke or systemic embolism by 19% and mortality by 10%, compared to warfarin.[17] With only a single stroke risk factor, oral anticoagulants (OAC) have a positive net clinical benefit (balancing stroke reduction and serious bleeding caused by OACs) when compared to no treatment or aspirin. Contrarily, the net clinical benefit for aspirin is neutral.[18] Therefore, concordant with current guidelines, OACs are the treatment of choice for preventing ischemic stroke in high-risk AF patients (defined as having a CHA_2DS_2-VASc score of ≥ 2[19]) and in a considerable proportion with a single stroke risk factor (CHA2DS2-VASc score = 1 in males).[20–22] These risk strata represent 95% of all AF patients.[23]

Notably, AF patients reap additional benefits from OACs, apart from ischemic stroke risk reduction. AF patients on warfarin with an INR ≥ 2 immediately before stroke have smaller brain infarcts[24,25] and lower stroke severity,[24] recurrence,[26] disability,[16,24,27–29] and mortality[16,27,29,30] relative to patients only taking antiplatelet agents, no antithrombotic drugs, or warfarin with an INR < 2.

Global underutilization of OACs in AF

The overwhelming scientific evidence has not translated into widespread use of OACs in AF patients. Globally, OACs are largely underutilized as roughly half of those with a clear indication are actually treated.[31,32] Even worse, utilization has not significantly changed in the last decade,[33–39] and although variable across geographic regions,[32–34,40] underutilization is a widespread global phenomenon.[32–34,37,40] Nonadherence to AF guidelines is also global and across all risk strata. Indeed, the proportion of nonadherence among the riskiest strata ranges from 33% to 68% (Middle East/Africa and Asia, respectively).[32] Particularly concerning in Asia, 60% of AF patients are prescribed antiplatelet drugs instead of OACs.[32,35] Worldwide, reasons for not prescribing oral anticoagulants feature poor risk stratification,[41,42] subjective over-interpretation of contraindications,[43] and variation between physicians' stated prescription preferences and actual prescription attitudes.[44] Emerging countries are unique in that additional predispositions to harm may warrant under-utilization of OACs, but scarce data in such areas contribute to slow integration of OAC use.[40,45]

Improving attitudes towards OAC utilization

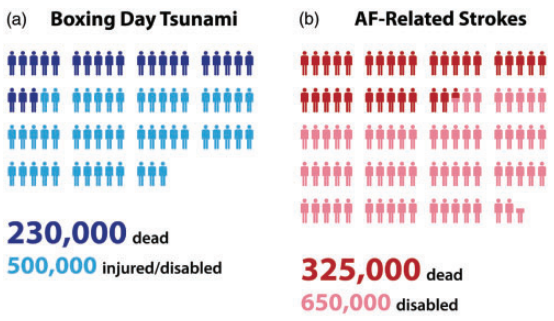
The framing effect

Most human decisions are unconscious and irrational, and greatly affected by how problems are framed.[46] The so-called "framing effect" (loss vs. gain frames) captures implicit effects of task-irrelevant emotional stimuli on decision-making. Since individuals react differently depending on how options are presented,[47,48] positive and benefit-based information is an important force of change in medicine.[49] For example, compared to loss-framed messages, gain-framing is more persuasive in promoting smoking cessation[50] and, furthermore, has been shown to be most preferred for heart disease medication counseling among 90% of patients surveyed.[51] A clinical decision to anticoagulate could function similarly. For the purpose of framing, physicians could explain the main possible outcomes of OACs for stroke prevention to their AF patients by using a well-balanced and intuitive concept such as "net clinical benefit". This comprehensive approach to translating evidence for patients should comprise the most relevant measures, while being transparent about both the benefits and risks of OACs (e.g. ischemic stroke prevention and bleeding risk from OAC use). Presenting the evidence as a combined metric may result friendlier for patients instead of multiple isolated outcomes. Also, a single net benefit measure would be simpler for physicians who have to incorporate large amounts of data from different drugs and clinical trials. When selecting a net clinical benefit measure for OACs, it has to be considered that they are chiefly prescribed to AF patients to prevent ischemic strokes. On the other hand, death and intracranial hemorrhage are the most feared safety outcomes both by patients and physicians.[52] This is despite considerable evidence depicting appreciably lower bleeding risk than ischemic stroke risk with OACs—more so with NOACs.[17] All other efficacy and safety outcomes are still important but are generally more benign and rarely associated with permanent disabling symptoms. Hence, a net clinical benefit outcome may include ischemic stroke, intracranial hemorrhage, and death. Importantly, OACs compared to no treatment result in a combined net clinical benefit of 50% lower risk of ischemic stroke, intracranial hemorrhage, and death, which clearly represents a "gain" frame.[53]

The AF-related stroke tsunami

Numbers per se are sometimes ineffective in conveying the magnitude of health problems to physicians and

Figure 1. (a) shows the estimated number of deaths and individuals injured within 30-days after the 2004 Boxing Day Tsunami in the Province of Aceh, Indonesia. (b) shows the hypothetical number of deaths and disabled patients 30 days after sustaining an AF-related stroke if none of the 33.5 million individuals living with AF globally were prescribed oral anticoagulants.



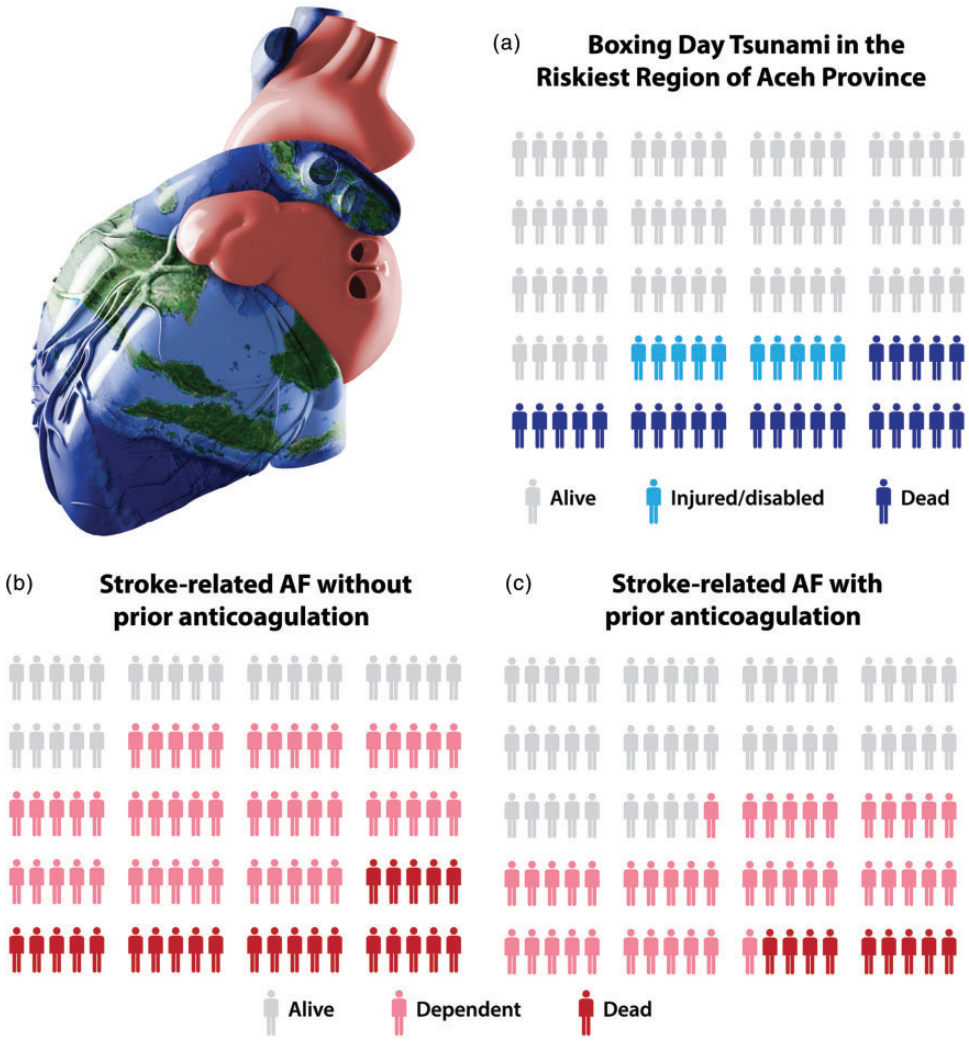
patients; however, they can potentially improve awareness in the context of meaningful and evocative events. Flashbulb memory helps to memorize and recall very specific details of circumstances in which individuals first learn of a very surprising or emotionally arousing event.[54,55] A typical "flashbulb event" is the World Trade Center 9/11 attack. Most people are able to recall their activities during 11 September 2001, but can hardly remember what they ate for dinner only 2 weeks ago. We propose that by comparing a major catastrophic flashbulb event to a hypothetical scenario in which all physicians ceased using OACs for stroke prevention in AF, it may help physicians and patients understand the negative consequences associated with OAC under-utilization and the magnitude to which OACs neutralize AF burden.

The Boxing Day Tsunami of 26 December 2004 affected 11 countries proximal to the Indian Ocean, killing over 230,000 people and injuring 500,000.[56] Among the latter, 1.4% (7000) remained permanently disabled.[57] Up to 170,000 deaths (74%) occurred in the epicenter of the tsunami, the Aceh province of Indonesia.[58] Over 97% of these deaths materialized within a 4-km distance of Aceh's coastline; this specific coastal region had a tsunami-related death rate of 23.7% within the next year,[57] while 10% of the survivors were injured.[58] A considerable proportion of these deaths occurred by drowning, the same day of the tsunami, followed by almost all remaining deaths within the following month.[56,59] The 30-day death rate of 23.7% in the epicenter of one of the top 3 deadliest natural catastrophes recorded in human history bears striking resemblance to the 30-day case-fatality rate of AF-related stroke, which ranges between 25% and 32.5%.[5,6,29,30] The difference is that the 2004 tsunami, which was responsible for 89% of deaths in all tsunamis occurring between 1900 and 2009,[59] required the energy equivalent of 23,000 Hiroshima-type atomic bombs, resulting in massive infrastructural destruction to match the magnitude of AF-related stroke mortality. If in an imaginary scenario, the 33.5 million individuals living with AF on the planet were left without OACs, but instead given aspirin, 1.3 million (4.0%/year)[15] would have an AF-related ischemic stroke during the following year. If left without any antithrombotic treatment, the number of strokes would raise to 1.5 million (4.5%/year).[15] Roughly, this would result in a death toll of 325,000 (25%[5,30] * 1.3 million) to 487,500 (32.5%[6] * 1.5 million) AF-related stroke patients and 650,000 (50%[16,30,39] * 1.3 million) to 750,000 (50%[16,30,39] * 1.5 million) being disabled 1 month after the stroke (Figure 1), culminating to more death and disability than the 2004 tsunami. With this comparison, we do not intend to make the Boxing Day tsunami look relatively harmless. Rather, we aim to illustrate how catastrophic AF could be without proper treatment.

Visual aids

Using visual aids to explain the implications of specific treatments may help patients better assimilate concepts.[60] Research efforts have focused on developing patient-centered decision-making instruments which empower patients to be involved in their own medical decisions.[61–63] Displaying benefits and risks of medication graphically was preferred by 57% of patients, which was 38 percentage points higher than the next preferred method (e.g. relative risk, absolute risk, or number needed to treat).[51] Furthermore, use of visual aids have the potential to eliminate the "framing effect" from patient decision-making.[64] Visual aids have been proposed as potential instruments to improve decision-making for intravenous thrombolysis and mechanical

Figure 2. Proportion alive, dependent, and dead in the Boxing Day Tsunami and after an AF-related stroke with and without prior anticoagulant treatment. (a) shows the proportion of the population who were estimated to be alive (65%), injured/ disabled (10%), and dead (25%) within 30 days after the 2004 Boxing Day Tsunami in the most devastated region of Aceh Province. (b) shows the proportion of AF patients without prior anticoagulants (only antiplatelet drugs, or warfarin but with an INR < 2, or no antithrombotic agents) estimated to be alive and without disability (25%), disabled (50%), and dead (25%) 30 days after an AF-related stroke. (c) shows the proportion of AF patients receiving warfarin with an INR > 2 estimated to be alive and without disability (49%), disabled (42%), and dead (9%) 30 days after an AF-related stroke.



Source: The design of the heart in this figure was created by combining images from Wikipedia (https://en.wikipedia.org/wiki/Heart#/media/File:Blausen_0456_Heart_Posterior.png) and Google Maps (Aceh Province map).

thrombectomy[62] in the hyper-acute stroke setting, as well for deciding oral anticoagulation in AF patients.[60] This information is presented as one possible rendition of visual aid, which may facilitate the process of counseling AF patients (Figure 2).

Prior research of AF thromboembolism prophylaxis, dated back to 1999, used decision aids to identify two key findings: (1) there is a gap between guideline recommendations and patient values and preferences, and (2) decision aids reduce the uncertainty of possible care alternatives so the patient can make an informed decision.[13] Furthermore, administration of oral anticoagulants that are in agreement with the developed decision aids actually prevent adverse events (stroke or major bleeds).[65] Future research evaluating the effectiveness of the decision aids for stroke prevention in patients with AF should include NOACs. A recent visual aid, formatted as a Cates plot, has been developed for

stroke prevention in patients with AF.[66] This aid was found to improve patient competency in terms of understanding the stroke and bleeding risk, and treatment alternatives, as well as enhancing the patient–physician interaction, but in fact did not change the treatment undertaken.[67] More recent renditions of visual aids have been published, but not yet studied for effectiveness in shared medical decision-making.[61,62] Visual aids also carry limitations. For instance, when reading the figure legends, patients whose first language is not English, may have difficulty in understanding these visual aids, unless translations are provided.

Conclusion

AF-related stroke is a highly preventable medical, social, and economic catastrophe. Up to now, drastic global efforts have led to inconsequential improvements in the proportion of patients treated with OACs. AF patients who have strokes because of not being prescribed OACs have a worse fate than individuals standing in the riskiest area of the Boxing Day tsunami's epicenter, waiting to be hit by the tsunami waves. Physicians' awareness and attitudes towards stroke prevention in AF require a radical change to tackle the AF-related stroke tsunami. Innovation to improve decision-making is timely required.

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Author contributions

JC wrote the first draft. JC, MM-O, AI, SD, and GYHL contributed with further content and edited the report. LAS conceived the idea, drafted the outline, edited the report, and designed the figures.

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