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Visual aid tools to assist the decision of Anticoagulation for Stroke Preventions.pdf

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Visual Aid Tool to Improve Decision Making in Anticoagulation for Stroke Prevention

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Background: The management of stroke prevention among patients with atrial fibrillation (AF) has changed in the last few years. Despite the benefits of new oral anticoagulants (NOACs), decisions about the optimal agent remain a challenge. We provide a visual aid tool to guide clinicians and patients in the decision process of selecting oral anticoagulants for stroke prevention. *Methods:* We created visual plots representing benefits of warfarin versus NOACs from a meta-analysis comprising 58,541 participants. Visual plots (Cates plots) were created using software available at nntonline.net. The primary outcome was stroke or systemic embolism during the study period. *Results:* In the chosen meta-analysis, 29,312 participants received a NOAC and 29,229 participants received warfarin. For every 1000 patients with AF, 38 would have a stroke or systemic embolic event in the warfarin group compared to 31 in the NOAC group (RR .81; 95% CI .73-.91). Fifteen patients would develop an intracranial hemorrhage in the warfarin group compared to 7 in the NOAC group (RR .48; 95% CI .39-.59). Conversely, 25 patients would develop gastrointestinal bleeding in the NOAC group compared to 20 in the warfarin group (RR 1.25; 95% CI 1.01-1.55). *Conclusion:* For every 1000 treated individuals with AF, NOACs would prevent stroke or systemic embolism in 7 additional patients and cerebral hemorrhage in 8 additional patients compared to warfarin. On the other hand, 5 more patients would develop gastrointestinal bleeding with NOACs compared to warfarin. These data are visually shown in Cates plots, facilitating conversations with patients regarding anticoagulation decisions. **Key Words:** Novel oral anticoagulation—visual aid tool—Cates plots—decision making.

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Background

The current management of atrial fibrillation (AF) for stroke prevention has recently changed with the publication of randomized controlled trials (RCTs) using new oral anticoagulants (NOACs). A recent meta-analysis from these RCTs consistently revealed the benefits of NOACs compared with warfarin in the prevention of stroke and systemic embolism.[1]

However, providing patients with the correct information to make an informed decision regarding anticoagulation remains a challenge around the world[2-4] because of lack of certainty, patient understanding, and communication methods.[5] One strategy for conveying choice information more simply and accurately involves graphical display, which can allow patients to rapidly understand the risks and benefits of a certain choice.[6]

One such visual aid, Cates plot (http://www.nntonline.net/visualrx/cates_plot),[7] is a decision tool created in 1999

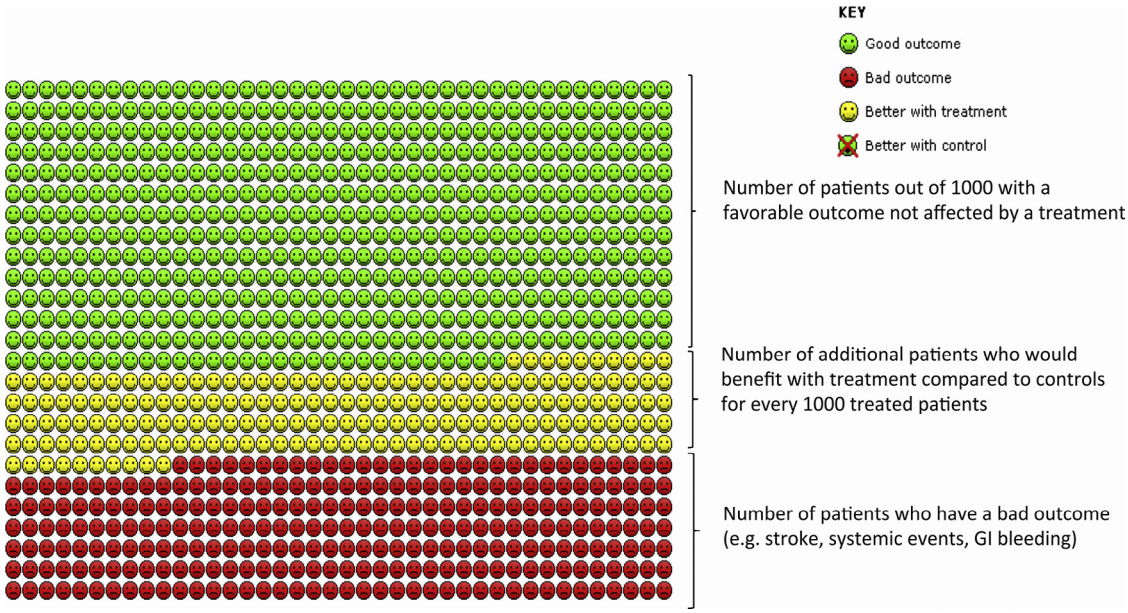

Figure 1. *Schematic interpretation of Cates plots. Abbreviation: GI, gastrointestinal.*

to visually illustrate and communicate the risks and benefits of treatments per 100 or 1000 patients. Here, we used the Cates plot to provide a visual aid tool to guide clinicians caring for patients with an acute ischemic stroke in making therapeutic decisions.

We chose to demonstrate NOAC efficacy and safety using the largest available meta-analysis,[1] as there is currently no available visual aid tool to discuss this complex topic with patients.

Methods

We created Cates plots derived from a recent meta-analysis of 4 large randomized trials comprising participants with AF assigned to receiving either NOACs or warfarin.[1]

Cates plots include 4 smiley face categories to visually depict the following: patients not affected by a treatment (green faces for those with a good outcome and red faces for those with a bad outcome); additional benefits of treatment compared to controls (yellow faces); and people with an adverse event that changes from a good outcome to a bad outcome (crossed-out green faces) (Fig 1). (Color version of figure is available online.) Cates plots were created with the available online calculator, by entering the event rate of the control group (warfarin), and relative risk of the intervention (NOACs) with 95% confidence intervals, obtained from Ruff et al.[1] The main outcome measure was stroke and systemic embolism. Safety outcomes included intracerebral hemorrhage and gastrointestinal bleeding. Mortality was a secondary outcome measure.

Results

Overall, 58,541 participants contributed to the estimates represented by the Cates plots. Although 42,411 patients were assigned to NOACs, only the higher doses of dabigatran and edoxaban were included in the meta-analysis, leaving 29,312 participants in the NOAC group (intervention group). 29,229 participants were assigned to standard warfarin (control group). The median follow-up was 1.8-2.8 years.[1] Table 1 summarizes the participants' characteristics.

For every 1000 patients with AF, 38 in the warfarin group would develop stroke or systemic embolism compared to 31 (RR .81; 95% CI .73-.91) in the NOAC group (Table 2, Fig 2, A). Differences based on $CHADS_2$ score and age are shown in Table 2 and Supplemental Materials.

Per 1000 patients, 15 would develop an intracranial hemorrhage in the warfarin group versus 7 in the NOAC group (RR .48; 95% CI .39-.59; Fig 2, B). However, there was a higher rate of gastrointestinal bleeding in the NOAC group (25 per 1000; RR 1.25; 95% CI 1.01-1.55) compared to the warfarin group (20 per 1000; Fig 2, B).

Discussion

The communication of the risk of stroke and complications related to anticoagulants constitutes a challenge for clinicians.[4,8] Previous studies showed that patients and physicians may misinterpret the risk of developing a medical condition or the expected response to a treatment.[9,10] Behavioral psychologists suggest the use of natural frequencies presented as visual aid decision tools to facilitate communication and understanding of risks in the real world.[9,11] Unfortunately, there are not many visual aid tools available to discuss therapeutic options, efficacy, and safety in stroke prevention.

In the present study, we introduced Cates plots as a visual aid tool to illustrate the risks and benefits of using

Table 1. *Baseline characteristic of participants included in the RCTs of NOACs versus warfarin*

	RE-LY			ROCKET-AF		ARISTOTLE		ENGAGE AF-TIMI 48			Combined	
	Dabigatran 150 mg (n = 6076)	Dabigatran 110 mg (n = 6015)	Warfarin (n = 6022)	Rivaroxaban (n = 7131)	Warfarin (n = 7133)	Apixaban (n = 9120)	Warfarin (n = 9081)	Edoxaban 60 mg (n = 7035)	Edoxaban 30 mg (n = 7034)	Warfarin (n = 7036)	NOAC (n = 42411)	Warfarin (n = 29272)
Age (years)	71.5 (8.8)	71.4 (8.6)	71.6 (8.6)	73 (65-78)	73 (65-78)	70 (63-76)	70 (63-76)	72 (64-68)	72 (64-78)	72 (64-78)	71.6	71.5
≥75 years	40%	38%	39%	43%	43%	31%	31%	41%	40%	40%	38%	38%
Women	37%	36%	37%	40%	40%	36%	35%	39%	39%	38%	38%	37%
Atrial fibrillation type												
Persistent or permanent	67%	68%	66%	81%	81%	85%	84%	75%	74%	75%	76%	77%
Paroxysmal	33%	32%	34%	18%	18%	15%	16%	25%	26%	25%	24%	22%
$CHADS_2$*	2.2 (1.2)	2.1 (1.1)	2.1 (1.1)	3.5 (0.94)	3.5 (0.95)	2.1 (1.1)	2.1 (1.1)	2.8 (0.97)	2.8 (0.97)	2.8 (0.98)	2.6 (1.0)	2.6 (1.0)
0-1	32%	33%	31%	0	0	34%	34%	<1%	<1%	<1%	17%	17%
2	35%	35%	37%	13%	13%	36%	36%	46%	47%	47%	35%	33%
3-6	33%	33%	32%	87%	87%	30%	30%	54%	53%	53%	48%	50%
Previous stroke or TIA*	20%	20%	20%	55%	55%	19%	18%	28%	29%	28%	29%	30%
Heart failure	32%	32%	32%	63%	62%	36%	35%	58%	57%	58%	46%	47%
Diabetes	23%	23%	23%	40%	40%	25%	25%	36%	36%	36%	31%	31%
Hypertension	79%	79%	79%	90%	91%	87%	88%	94%	94%	94%	88%	88%
Prior myocardial infarction	17%	17%	16%	17%	18%	15%	14%	11%	12%	12%	15%	15%
Aspirin at baseline	39%	40%	41%	36%	37%	31%	31%	29%	29%	30%	34%	34%
Median follow-up (years)	2.0	2.0	2.0	1.9	1.9	1.8	1.8	2.8	2.8	2.8	2.2	2.2
Individual mean TTR	NA	NA	67 (54-78)	NA	58 (43-71)	NA	66 (52-77)	NA	NA	68 (57-77)	NA	65 (51-76)

Abbreviations: CHADS2, stroke risk factor scoring system in which 1 point is given for history of congestive heart failure, hypertension, age ≥75 years, and diabetes, and 2 points are given for history of stroke or transient ischemic attack; NA, not available; NOAC, new oral anticoagulant; RCT, randomized controlled trial; TIA, transient ischemic attack; TTR, time in therapeutic range.

Data are mean (SD), median (IQR), or percent, unless otherwise indicated.

*ROCKET-AF and ARISTOTLE included patients with systemic embolism.

Reproduced with permission from Ruff et al.[1]

Table 2. *Comparison of outcomes between NOACs and warfarin based on the meta-analysis of 4 RCTs*[1]

Outcome measures	Events		Number of patients affected per 1000		RR (95% CI)	*P* value
	NOACs n/N	Warfarin n/N	NOACs	Warfarin		
Primary outcome						
Stroke or systemic embolism	911/29,312	1,107/29,229	31	38	.81 (.73-.91)	<.0001
Stroke or systemic embolism by $CHADS_2$ score						
$CHADS_2$ = 0-1	69/5,058	90/4,942	14	18	.75 (.54-1.04)	.072
$CHADS_2$ = 2	247/9,563	290/9,757	26	30	.86 (.70-1.05)	.109
$CHADS_2$ = 3-6	596/14,690	733/14,528	41	51	.80 (.72-.89)	<.0001
Stroke and systemic embolism by age						
<75	496/18,073	578/18,004	27	32	.85 (.73-.99)	.011
≥75	415/11,188	532/11,095	37	48	.78 (.68-.88)	<.0001
Secondary outcomes						
Intracranial hemorrhage	204/29,287	425/29,211	7	15	.48 (.39-.59)	<.0001
Gastrointestinal bleeding	751/29,287	591/29,211	25	20	1.25 (1.01-1.55)	.043
Mortality	2,022/29,292	2,245/29,221	69	77	.90 (.85-.95)	.0003

Abbreviations: NOAC, new oral anticoagulant; RCT, randomized controlled trial.

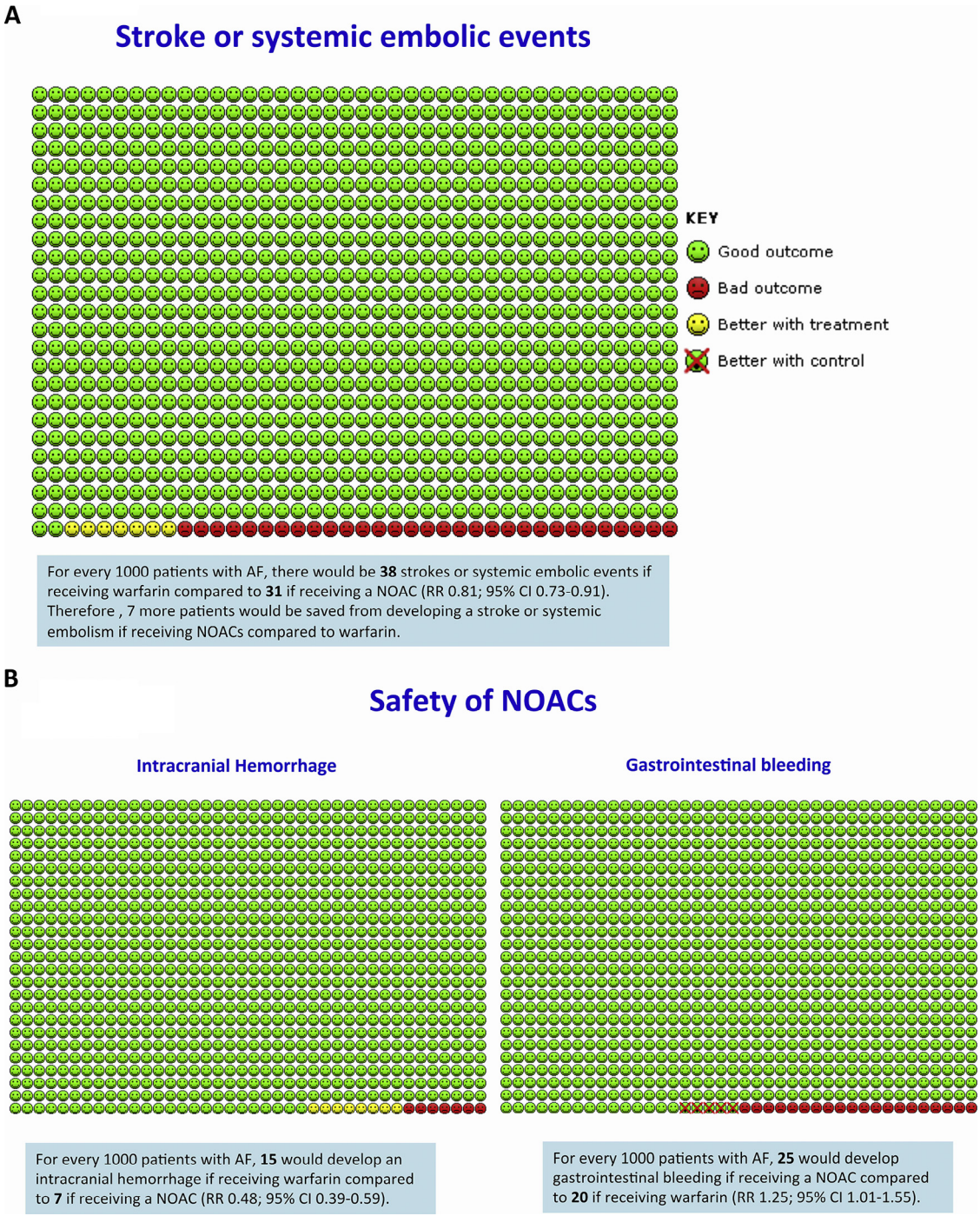

Figure 2. *(A) Cates plots demonstrating risk of stroke and systemic embolism between warfarin (control) and NOAC (intervention) groups. (B) Cates plots demonstrating intracranial and gastrointestinal hemorrhages between warfarin (control) and NOAC (intervention) groups. Abbreviations: AF, atrial fibrillation; NOAC, new oral anticoagulant.*

a NOAC versus warfarin. The figures visually demonstrated the advantage of NOACs over warfarin in all categories except gastrointestinal hemorrhage. The use of visual tools providing information on gains and losses of diagnostic or therapeutic options has been shown to change and improve decision making.[12,13] For example, Man-Son-Hing et al applied a similar approach to 287 patients participating in the SPAF III aspirin cohort study. Compared with patients in the usual care group, those who used the decision aid tool were more likely to make a decision regarding antithrombotic therapy (aspirin or warfarin), were more knowledgeable, and had more realistic expectations.[14]

Our main limitation is the lack of supporting evidence that such an approach can improve decision making in patients considered for anticoagulation. The next step

would be to validate the effect of visual aid tools at the bedside on rates of warfarin and NOAC prescriptions, and the subjective clinician and patient experiences in making a decision. Another limitation is the inability to visually portray less tangible outcomes, such as the advantage of foregoing international normalized ratio checks with NOACs, or current easier reversibility of warfarin. Lastly, the data do not take into account individual risk profiles, such as patients with high risk of gastrointestinal bleeding.

In conclusion, stroke prevention in the context of AF represents a challenge for decision makers due to a variety of treatment options. Conveying accurate information regarding the expected outcome is crucial when counseling stroke patients and their families. Cates plots represent a step forward to promptly facilitate information sharing using a visual aid tool and guide therapeutic options in acute stroke care.

Appendix: Supplementary material

Supplementary data to this article can be found online at doi:10.1016/j.jstrokecerebrovasdis.2016.05.037.

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