

## Novel tool for predicting residual stroke risk in atrial fibrillation: mCARS

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**Background:** Recently, CARS was proposed to predict 1-year absolute stroke risk in non-anticoagulated patients with atrial fibrillation (AF). We aimed to determine whether a modified CARS (mCARS) may be used to assess the residual stroke risk in anticoagulated AF patients.

**Methods:** We studied patient-level data of anticoagulated AF patients from the real-world Murcia AF Project and AMADEUS clinical trial. Individual mCARS was estimated for each patient using an estimated 64% risk reduction with anticoagulation.

**Results:** 3,503 patients were included (2,205 [62.9%] clinical trial and 1,298 [37.1%] real-world). In the clinical trial cohort, the median age was 71 (IQR 65-77) and CHA<sub>2</sub>DS<sub>2</sub>-VASc score 3 (IQR 2-4). In the real-world cohort, the median age was 76 (IQR 70-81) and CHA<sub>2</sub>DS<sub>2</sub>-VASc score 4 (IQR 3-5).

At 1-year, there were 40 and 31 stroke events in the clinical trial and real-world cohorts, respectively. Average predicted residual stroke risk by mCARS was identical to actual stroke risk (1.8 [±1.8%] vs. 1.8% [95% CI, 1.3-2.4]) in the clinical trial, and broadly similar in the real-world (2.1 [±1.9%] vs. 2.4% [95% CI, 1.6-3.4]). Additionally, these values were comparable across the subgroups stratified by CHA<sub>2</sub>DS<sub>2</sub>-VASc score in both cohorts.

AUCs of mCARS for prediction of stroke events in the clinical trial and real-world were 0.678 (95% CI, 0.598-0.758) and 0.712 (95% CI, 0.618-0.805), respectively. In an exploratory analysis, we found that mCARS was able to refine stroke risk estimation for each point of the CHA<sub>2</sub>DS<sub>2</sub>-VASc score in both cohorts.

**Conclusion:** Personalised residual 1-year absolute stroke risk in anticoagulated AF patients may be estimated using mCARS. Such patients with high residual stroke risk may benefit from more aggressive interventions and follow-up.

Absolute 1-year stroke risk

	Clinical Trial		Real-World	
	Median (IQR)	Range	Median (IQR)	Range
CHA <sub>2</sub> DS <sub>2</sub> -VASc score 0	NA		0.9 (0.6 - 1.3)	0.2 - 1.4
CHA <sub>2</sub> DS <sub>2</sub> -VASc score 1	1.1 (0.7 - 1.4)	0.2 - 2.0	1.4 (0.9 - 1.7)	0.2 - 13.0
CHA <sub>2</sub> DS <sub>2</sub> -VASc score 2	2.0 (1.5 - 2.4)	0.3 - 10.8	2.1 (1.5 - 2.6)	0.3 - 10.8
CHA <sub>2</sub> DS <sub>2</sub> -VASc score 3	2.6 (2.1 - 3.4)	0.4 - 13.3	2.8 (2.5 - 3.4)	0.9 - 13.3
CHA <sub>2</sub> DS <sub>2</sub> -VASc score 4	3.6 (2.8 - 5.6)	0.3 - 18.1	3.9 (3.3 - 5.0)	1.1 - 21.0
CHA <sub>2</sub> DS <sub>2</sub> -VASc score 5	6.7 (3.6 - 14.0)	1.9 - 20.9	4.8 (3.9 - 12.2)	1.2 - 21.0
CHA <sub>2</sub> DS <sub>2</sub> -VASc score 6	13.6 (5.5 - 15.8)	2.4 - 21.8	12.8 (4.8 - 16.7)	2.2 - 21.8
CHA <sub>2</sub> DS <sub>2</sub> -VASc score 7	15.7 (14.5 - 17.4)	4.5 - 21.9	15.6 (5.9 - 17.5)	4.1 - 23.5
CHA <sub>2</sub> DS <sub>2</sub> -VASc score 8	16.5 (14.0 - 18.5)	13.1 - 20.3	16.9 (15.7 - 19.5)	13.6 - 21.0

IQR, interquartile range; NA, not applicable.