

**Background:** Despite a relatively simple tool for categorizing stroke risk in patients with atrial fibrillation, there still remains many questions regarding the definitions and inclusions of certain components of the CHA2DS2-VASc Score (Table 1). The validation trial of this score was published in 2010; therefore, the original definitions of the individual components as outlined in this trial have been modified throughout time and with subsequent anticoagulation trials as discussed below. This tool leaves much room for individual interpretation, and its use within anticoagulation decisions emphasizes a need for a joint discussion between patient and provider. Below is a summary of the more controversial components of the CHA2DS2-VASc score within nonvalvular atrial fibrillation (AF)<sup>1-4</sup> Landmark trials for approval of DOACs included up to 20% of patients who had some type of valvular defects<sup>5</sup>

Table 1 The CHA2DS2-VASc Score <sup>1</sup>			Table 2 Heart Failure Definitions within DOAC Trials		
Risk Factor	Score	Definition	Trial	Anticoagulant	Heart Failure Definition
Congestive Heart Failure/LV dysfunction	1	Left ventricular dysfunction or symptomatic heart failure	RE-LY <sup>2</sup>	Dabigatran	Symptomatic heart failure 6 months prior to enrollment or a previous history of heart failure admission
Hypertension	1	More than 140/90mmHg (use of 130/80mmHg is acceptable) or on antihypertensive therapy			
Age ≥ 75 years old	2		ROCKET-AF <sup>3</sup>	Rivaroxaban	Previous history of heart failure or left ventricular dysfunction defined as an ejection fraction of < 40%
Diabetes Mellitus	1	Fasting blood glucose > 126 mg/dL, HgA1c > 6.5%, or receiving treatment for diabetes			
Stroke/TIA/TE	2	Prior history of stroke, TIA, or systemic embolism	ARISTOTLE <sup>4</sup>	Apixaban	Ejection fraction ≤ 40% or symptomatic heart failure within the 3 months prior to enrollment
Vascular disease	1	Prior myocardial infarction (MI), angina pectoris, percutaneous coronary intervention or coronary artery bypass surgery, intermittent claudication, previous surgery or percutaneous intervention of the abdominal aorta or lower extremity vessels, abdominal or thoracic surgery, arterial and venous thrombosis			
Age 65-74 years old	1		ENGAGE-AF <sup>5</sup>	Edoxaban	Symptomatic heart failure or a history of heart failure admission regardless of ejection fraction
Sex category (female gender)	1				

Detailed Definitions of CHADSVASC Components	
Risk Factor	Definition
Heart Failure	The original definition was adopted from the CHADS2 score and states that heart failure is "the presence of signs and symptoms of either right or left ventricular failure or both, confirmed by non-invasive or invasive measurements demonstrating objective evidence of cardiac dysfunction". When looking at more recent atrial fibrillation trials with direct-oral anticoagulants (DOAC), each trial had their own definition of heart failure (see Table 2). Looking at all of the definitions in totality, it is acceptable to include left ventricular dysfunction (an ejection fraction of < 40%) and symptomatic heart failure with diagnostic evidence of ventricular failure regardless of ejection fraction within the CHA2DS2-VASc score.
Hypertension	The original definition of hypertension is a resting systolic blood pressure of > 140mmHg and/or a diastolic blood pressure of > 90 mmHg on at least 2 occasions, or currently on antihypertensive treatment <sup>1</sup> . In 2017, the definition and classification of hypertension changed as evidence emerged in favor of stricter blood pressure targets. Hypertension is now defined as a systolic blood pressure of > 130 mmHg and/or a diastolic blood pressure of > 80 mmHg, or currently on antihypertensive treatment <sup>6</sup> . Given this update, it is reasonable to include any patient with a diagnosis of hypertension (using a threshold of 130/80 mmHg or 140/90 mmHg) or on antihypertensive treatment.
Diabetes	The original definition was a fasting glucose of > 126 mg/dL or actively receiving treatment for diabetes <sup>1</sup> . Hemoglobin A1c has emerged as another way of diagnosing diabetes. According to the ADA guidelines, a hemoglobin A1c of > 6.5% is diagnostic of diabetes <sup>7</sup> . This is a reasonable method to be included into the CHA2DS2-VASc score.
Stroke/TIA/Thromboembolism (TE):	The confusion within this component of the CHA2DS2-VASc score comes from the inclusion of TE. There are several areas within the original validation trial that would infer that deep vein thrombosis (DVT) or pulmonary embolism (PE) would be included within the score <sup>1</sup> . A key point in clarifying this component is to define "systemic embolism". The term "systemic" implies that the clot develops in the left-side of the heart and the embolism will be pushed "systemically" or via the arteries. Specifically, the ARISTOTLE trial defined systemic embolism as requiring "a clinical history consistent with an acute loss of blood flow to a peripheral artery (or arteries) supported by the evidence of embolism from surgical specimens, autopsy, angiography, vascular imaging, or other objective testing." <sup>4</sup> By these definitions, DVT and PE would not be included within the CHA2DS2-VASc score; however, a DVT and/or PE identifies a high-risk population for recurrent embolisms and might need to be evaluated independently in clinical decisions within anticoagulation therapy <sup>8</sup> .
Vascular Disease	Within the definitions of the original trial, "coronary artery disease" was abbreviated to "prior MI," but it really includes "prior myocardial infarction (MI), angina pectoris, percutaneous coronary intervention or coronary artery bypass surgery." Another discrepancy seen within the validation trial was the use of "peripheral artery disease" within the score, but in the supplement, they defined peripheral vascular disease, which encompasses more conditions than peripheral artery disease. It was defined as "intermittent claudication [symptomatic peripheral artery disease], previous surgery or percutaneous intervention of the abdominal aorta or lower extremity vessels, abdominal or thoracic surgery, arterial and venous thrombosis" <sup>1</sup> . Given the broad definition of vascular disease, there is a lot of room for individual interpretation and a joint discussion between provider and patient regarding anticoagulation decisions might be needed.

#### References:

- Lip, GYH, Nieuwlaar R, Pisters R. Redefining Clinical Risk Stratification for Predicting Stroke and Thromboembolism in Atrial Fibrillation Using a Novel Risk Factor-Based Approach. Chest 2010; 137(2), 263-72. DOI: 10.1378/chest.09-1584
- Connolly SJ, Ezekowitz MD. Dabigatran versus Warfarin in Patients with Atrial Fibrillation. N Engl J Med 2009; 361:1139-1151. DOI: 10.1056/NEJMoa0905561
- Patel MR, Mahaffey KW, Garg J. Rivaroxaban versus Warfarin in Nonvalvular Atrial Fibrillation. N Engl J Med 2011; 365:883-891. DOI: 10.1056/NEJMoa1009638
- Hohnloser SH, Fudim M, Alexander JH, et al. Efficacy and Safety of Apixaban Versus Warfarin in Patients With Atrial Fibrillation and Extremes in Body Weight: Insights From the ARISTOTLE Trial. Circulation 2019;139:2292-300.
- Giugliano RP, Ruff CT, Braunwald E. Edoxaban versus Warfarin in Patients with Atrial Fibrillation. N Engl J Med 2013; 369:2093-2104. DOI: 10.1056/NEJMoa1310907
- Whelton PK, Carey RM, Aronow WS. 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APHA/ASH/ASPC/PCNA Guidelines for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. Hypertension 2018; 71(6): e13-e115. DOI: 10.1161/HYP.0000000000000065
- American Diabetes Association. Classification and diagnosis of diabetes: Standards of Medical Care in Diabetes 2019. Diabetes Care 2019;42(Suppl. 1):S13-S28
- Kearon C. Circulation. Natural history of venous thromboembolism. Circulation 2003;107:1-22-1-30