

APPENDIX 1

Definitions used in the BALKAN-AF Survey

Acute coronary syndrome – *i*) acute coronary syndrome with ST segment elevation - acute chest pain with persistent (>20 min) ST-segment elevation or (presumably) new left bundle branch block, *ii*) acute coronary syndrome without persistent ST segment elevation - acute chest pain with persistent or transient ST-segment depression or T-wave inversion, flat T waves, pseudo-normalization of T waves, or no ECG changes; if rise/fall in cardiac troponins was registered, acute coronary syndrome without persistent ST segment elevation was designated as non-ST elevation myocardial infarction, while normal troponin levels denoted unstable angina pectoris (1).

Stable coronary artery disease – episodes of reversible myocardial demand/supply mismatch, related to ischemia or hypoxia, which are usually inducible by exercise, emotion or other stress and reproducible — but, which may also be occurring spontaneously (2).

Hypertension – ≥ 140 mmHg systolic blood pressure and/or ≥ 90 mmHg diastolic blood pressure at office measurement (3).

Heart failure – symptoms (e.g. breathlessness, ankle swelling, fatigue) and signs (elevated jugular venous pressure, pulmonary crackles, and displaced apex beat) resulting from an abnormality of cardiac structure or function (4).

New York Heart Association (NYHA) classification - **Class I:** No limitation of physical activity. Ordinary physical activity does not cause undue breathlessness, fatigue, or palpitations. **Class II:** Slight limitation of physical activity. Comfortable at rest, but ordinary physical activity results in undue breathlessness, fatigue, or palpitations. **Class III:** Marked limitation of physical activity. Comfortable at rest, but less than ordinary physical activity results in undue breathlessness, fatigue, or palpitations. **Class IV:** Unable to carry on any physical activity without discomfort. Symptoms at rest can be present. If any physical activity is undertaken, discomfort is increased (4).

Valvular heart disease – intrinsic lesions affecting one or several components of the native heart valve apparatus including mild to moderate native heart valve stenosis, prolapse or regurgitation (5).

Dilated cardiomyopathy – ventricular enlargement and ventricular systolic dysfunction in the absence of significant coronary artery disease (6).

Hypertrophic cardiomyopathy - the presence of increased left ventricular wall thickness that is not solely explained by abnormal loading conditions (7).

Restrictive cardiomyopathy – impaired ventricular diastolic filling due to excessive rigidity of ventricular walls, without impairment of systolic function or evidence of pericardial disease (6).

Congenital heart disease – abnormality of cardiocirculatory structure and/or function that is present at birth, even if discovered later in life (8).

AF clinical type - *First diagnosed AF*: patients who presented with AF for the first time, irrespective of AF duration before diagnosis. *Paroxysmal AF*: self-terminating AF episodes, usually lasting 48 h - 7 days. *Persistent AF*: an AF episode that lasts longer than 7 days or requires termination by cardioversion, either with drugs or by direct current cardioversion. *Long-standing persistent AF*: AF that has persisted for ≥ 1 year when it is decided to adopt a rhythm control strategy and attempt AF termination by cardioversion. *Permanent AF*: the presence of permanent AF is accepted by the patient and the physician and rhythm control interventions are not further pursued (9).

EHRA symptom classification - *EHRA I*: ‘No symptoms’; *EHRA II*: ‘Mild symptoms’ - normal daily activity not affected; *EHRA III*: ‘Severe symptoms’; normal daily activity affected; *EHRA IV*: ‘Disabling symptoms’; normal daily activity discontinued (9).

CHADS₂ score – *C* - congestive heart failure; *H* – arterial hypertension; *A* - age ≥ 75 years; *D* – diabetes mellitus; *S₂* – history of stroke or transient ischemic attack. Two points are assigned for a history of stroke or transient ischemic attack and 1 point each is assigned for age ≥ 75 years, a history of hypertension, diabetes, or heart failure (9).

CHA₂DS₂-VASc score - *C* - congestive heart failure or left ventricular systolic dysfunction (left ventricular ejection fraction $\leq 40\%$); *H* – arterial hypertension; *A₂* - age ≥ 75 years; *D* – diabetes mellitus; *S₂*– history of stroke or transient ischemic attack; *V* – vascular disease (prior myocardial infarction, peripheral artery disease, aortic plaque); *A* – age 65-74 years; *Sc* – sex category – female. Two points are assigned for a history of stroke or transient ischemic attack, or age ≥ 75 ; and 1 point each is assigned for age 65–74 years, hypertension, diabetes, heart failure/left ventricular systolic dysfunction, vascular disease and female sex (9).

HASBLED score – *H* – hypertension (defined as systolic blood pressure ≥ 160 mmHg); *A* – Abnormal kidney function (presence of chronic dialysis or renal transplantation or serum creatinine ≥ 200 mmol/L. and or abnormal liver function (chronic hepatic disease such as cirrhosis or laboratory abnormalities denoting significant hepatic derangement such as bilirubin ≥ 2 x upper limit of normal, in association with aspartate aminotransferase/alanine aminotransferase/alkaline phosphatase ≥ 3 x upper limit normal); *B* – bleeding (previous bleeding events and/or predisposition to bleeding such as bleeding diathesis, anaemia, etc.); Labile International Normalized Ratios (INR) (unstable/high INRs or time in therapeutic range $\leq 60\%$); *D* - drugs/alcohol use (concomitant use of drugs, such as antiplatelet agents, non-steroidal anti-inflammatory drugs, or alcohol abuse). One point each is assigned for any of the HASBLED score components (9).

Peripheral arterial disease – atherothrombotic disease of the carotid, vertebral, upper extremity, mesenteric, renal, and lower extremity arterial vessels (10).

Sleep apnea – repetitive collapse of the upper airway during sleep with chronic intermittent hypoxia and recurrent arousals (11).

COPD – persistent airflow limitation that is usually progressive and associated with an enhanced chronic inflammatory response in the airways (12).

Anaemia – Haemoglobin level in non-pregnant women < 120 g/L and men < 130 g/L (13).

Diabetes mellitus – fasting plasma glucose ≥ 7.0 mmol/L, and/or 2-h post-load plasma glucose ≥ 11.0 mmol/L, and/or HbA_{1c} $\geq 6.5\%$ (14).

Chronic kidney disease - kidney damage, as evidenced by the presence of a structural abnormality or persistent hematuria and/or proteinuria, and/or reduced kidney function, as determined by a decreased glomerular filtration rate (eGFR <60 mL/min/1.73 m²) (15).

Chronic liver disease - patients presenting with signs and symptoms of chronic liver disease or has risk factors for chronic liver disease (e.g., alcohol abuse, risk of viral hepatitis, obesity) with confirmed laboratory abnormalities (e.g., elevated aspartate aminotransferase/alanine aminotransferase) or positive screen for serologic markers of liver disease (16).

Thyroid disease - *Hyperthyreosis* : TSH below the lower limit of normal and FT4 and FT3 above the upper limit of normal; *Hypothyreosis*: TSH above the upper limit of normal and FT4 and FT3 below the lower limit of normal

Malignancy –confirmed solid organ or hematological malignancy currently under treatment or previously treated and considered as cured.

Stroke - a focal neurologic deficit, from a nontraumatic cause, lasting at least 24 hours, categorized as ischemic (with or without hemorrhagic transformation), hemorrhagic, or of uncertain type (in the case of patients who did not undergo brain imaging or in whom an autopsy was not performed) (17).

Transient ischemic attack - a focal neurologic deficit, from a nontraumatic cause, lasting less than 24 hours (17).

Peripheral embolism – clinical history consistent with an acute loss of blood flow to a peripheral artery (or arteries) supported by evidence of embolism from surgical specimens, autopsy, angiography, vascular imaging, or other objective testing (17).

Bleeding - *ISTH definition of major bleeding*: i) Fatal bleeding, and/or ii) symptomatic bleeding in a critical area or organ, such as intracranial, intraspinal, intraocular, retroperitoneal, intraarticular or pericardial, or intramuscular with compartment syndrome, and/or iii) bleeding causing a fall in hemoglobin level of 20 g/L or more, or leading to transfusion of two or more units of whole blood or red cells (18). *Clinically relevant nonmajor bleeding* - clinically overt bleeding that did not satisfy the criteria for major bleeding and that led to hospital admission, physician-guided medical or surgical treatment, or a change in antithrombotic therapy (17).

Pulmonary embolism - confirmed by computed tomography-pulmonary angiogram in the presence of clinical symptoms (e.g. dyspnoea, chest pain, pre-syncope or syncope, and/or haemoptysis), electrocardiographic and laboratory abnormalities (e.g. elevated serum levels of D-dimer) (19).

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